Milk testing for residues to ensure quality products

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Main Residues Currently

- Iodine
- Trichloromethane
- Flukicides
- Quaternary ammonium compounds (QACs)
- DEHP
- Chlorates

Iodine

- Iodine is an essential trace element - humans and animals
- Deficiency affects reproductive capacity, brain development and growth
- Increased iodine content in food due to greater use in:
  - food processing, animal rations, antimicrobial agents
- Whole milk and dairy products contribute highest proportion of iodine to the human diet
- Human requirements:
  - US Food and Nutrition Board (2001) :
    - Adult - 150 μg/day; children - 110 - 130 μg/day
  - German nutritional reference point (DACH, 2000) :
    - Adult - 180-200 μg/day; children - 40 – 80 μg/day

- **Average: Adult : 170 μg/day; children : 90 μg/day**

Why is milk iodine a quality issue

- Ireland – major exporter of dairy products
- Milk quality is critical to maintaining and expanding this market
- Ireland is one of leading infant formula manufacturers worldwide
- Market has significant potential for growth
- Two mechanisms :
  - Milk powder as an ingredient can be sourced abroad
  - Milk powder can be produced and sourced at home
    - Preferable
    - Needs to have correct levels and balance of minerals including iodine
- Target for iodine in milk powder as an ingredient in IMF :
  - 100 μg iodine/ 100g powder
  - equates to <250 μg iodine/kg milk
- Difficult to source at times of year, e.g. - concentrations of >500 μg/kg recorded for December (O'Brien *et al*. 1999, 2013)

Iodine sources that can lead to high milk iodine

1. Concentrate feed

- Early 1990s – 139 µg iodine/kg milk; 97% of pasture samples – subnormal iodine levels
- Recommended adequate supplementation of iodine
- 12-60 mg of iodine /cow per day
  - ~12 mg of iodine /cow per day advised for routine continuous use
  - ~60 mg of iodine /cow per day advised for national use in a 5-month mineral programme for dairy cows

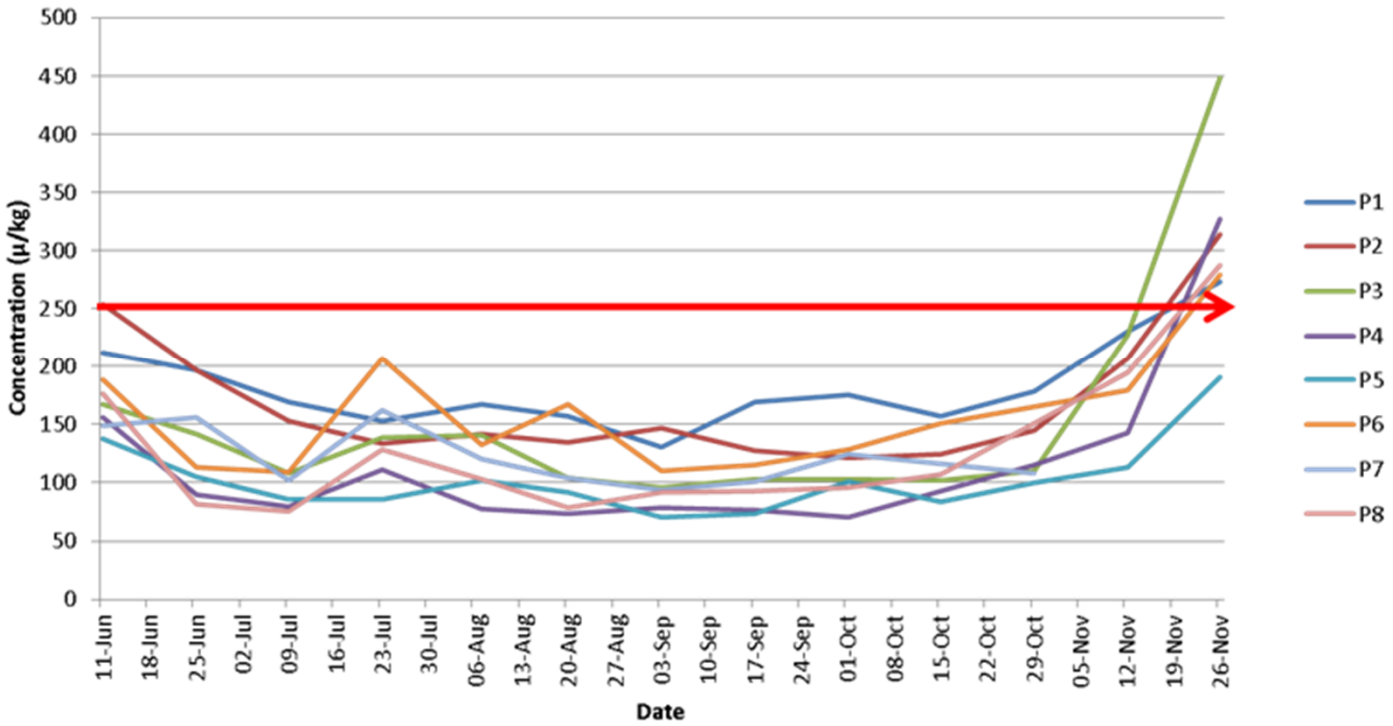
2. Teat disinfection

- Used as a routine practice on-farm post-milking, and potentially pre-milking
- Contribution of post- disinfection iodine to milk iodine may be due to absorption through skin
- In Irish scenario – same strength pre and post milking
- Pre-milking disinfection can pose a substantial risk of iodine transfer to milk
- Dependent on the degree of removal from the teats prior to cluster attachment

High iodine intake risks

- **0.5mg/kg DM** intake or approximately 10-12 mg/cow/day
- High milk iodine may be exacerbated by seasonal milk production
- Two situations particularly at risk:
  - Early lactation cows in a spring system
  - Winter milking cows
- Iodine routinely added to feed rations at 5-10 mg/kg
- Cows typically fed 6-7 kg/cow/day in early lactation – can deliver 60-70 mg/cow/day
- Level of iodine in feed set a/c to the volume fed
- Excess iodine intake by cows excreted into milk & urine

Iodine concentrations for 8 processor milks at 13 dates -2013



Conclusions

- Recommended supplementation level a/c to animal research documentation is 0.5 mg/kg DM/cow/day or ~10 – 12 mg/kg/cow/day
- Supplementation levels up to 60 mg/cow/day (up to 6 x)
- Seasonal problem in Ireland; early lactation spring and winter milk production
- Milk iodine level is most important in areas where milk is destined for IMF
- At a limit of 250 µg/kg – little flexibility
- Methodology now set up at Moorepark – ICPMS
- Can monitor more closely – monthly milk sample collection – national perspective
- Supplement more precisely to meet requirement

Flukicides

Aim of Research

To determine the presence of veterinary drug residues, following their administration to lactating cows, in milk and milk products and their stability within such products

Advances in analytical technology for the analysis of flukicide residues in milk

More precise monitoring of milk and other foodstuffs

Procedures have identified residues of a number of flukicides in milk. The flukicides involved do not have a Maximum Residue Limit applied to them. In the absence of an MRL, any measurable level of the flukicide should not be present

<u>On-farm</u>

- Only 3 active ingredients
  - Albendazole (Liver Fluke only)
  - Oxyclozanide (Liver and Rumen Fluke)
  - Triclabendazole
- Will require minimum of 2 doses
- Third Dose probably required

Control

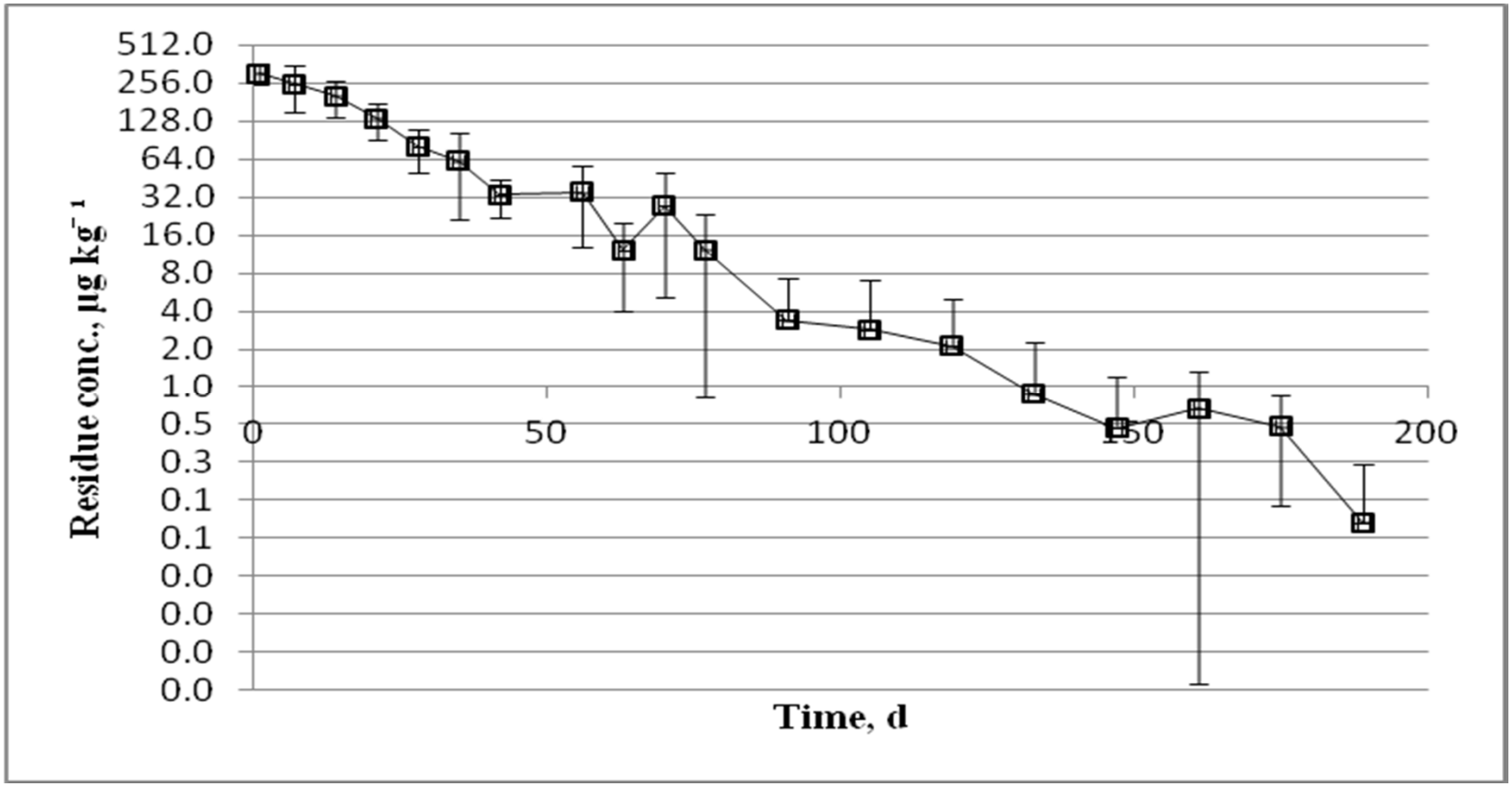
MEDICINES THAT CAN CONTINUE TO BE USED WITH STRICT ADHERENCE TO WITHDRAWAL PERIODS INDICATED	
Name of product	Active ingredient
Albex 10%	**Albendazole**
Albex 2.5%	**Albendazole**
Endospec 10% SC	**Albendazole**
Endospec 2.5% SC	**Albendazole**
Keelogane SC	**Albendazole**
Osmonds Flexiben 10% SC	**Albendazole**
Tramazole 10%	**Albendazole**
Tramazole 2.5%	**Albendazole**
Valbazen 10%	**Albendazole**
Fasinex 240	**Triclabendazole**
Endofluke 100 mg/ml	**Triclabendazole**
Fasifree 10%	**Triclabendazole**
Zanil	**Oxyclozanide**

Pharmacologicals remain the mainstay of control
Only active against mature adult fluke

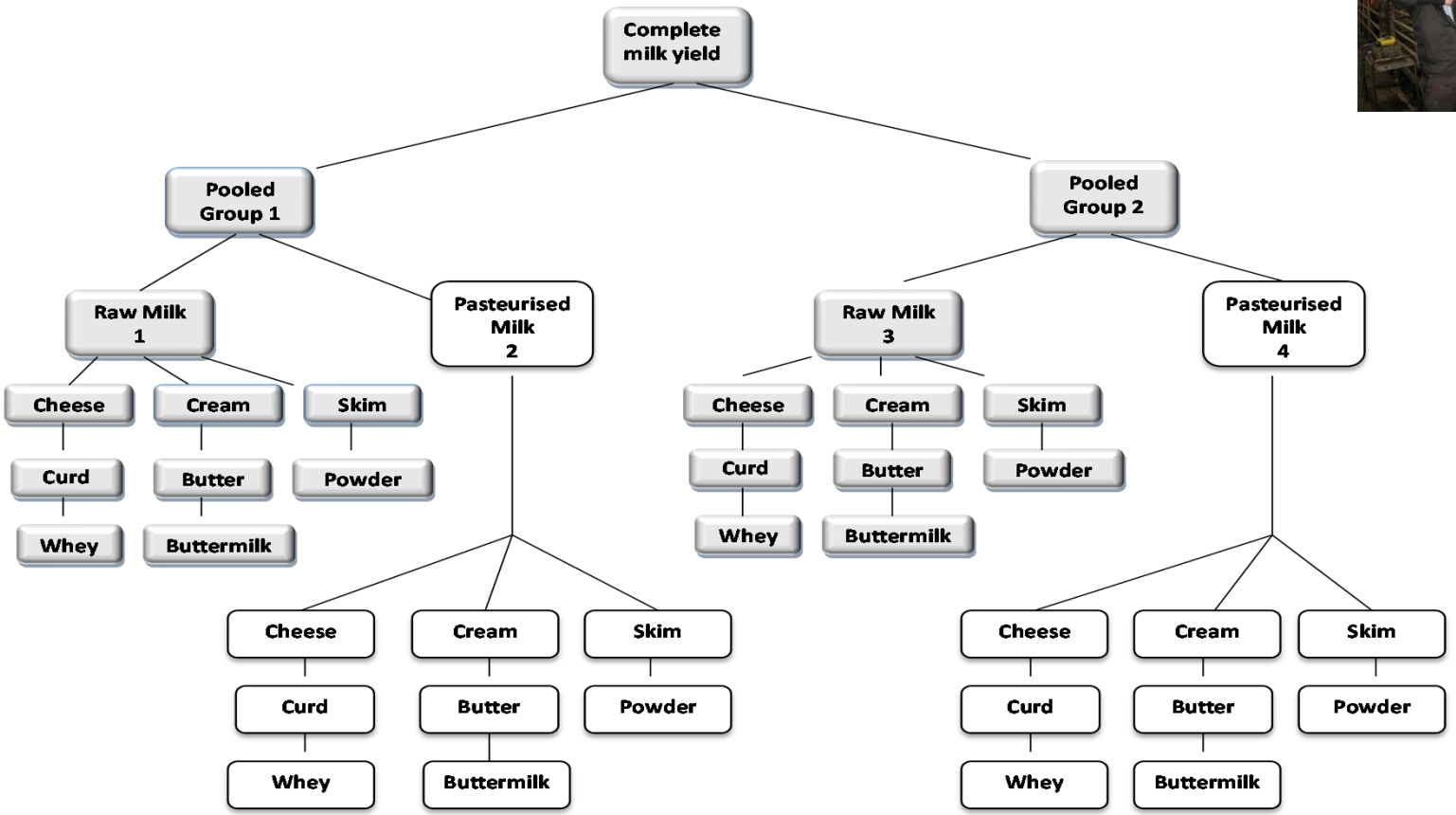
Be Careful!

MEDICINES NOT TO BE ADMINISTERED TO COWS/IN-CALF HEIFERS			
Name of product	Active substance	Name of product	Active substance
Virbamec super	Clorsulon	Rafazole Oral Suspension	Rafoxanide
Ivomec super	Clorsulon	Ridafluke 3%	Rafoxanide
Flukiver 5 Injection	Closantel	Univet Multidose Fluke and Worm	Rafoxanide
Closamectin	Closantel	Flukex 3%	Rafoxanide
Closiver for cattle	Closantel	Flukex 9%	Rafoxanide
Closamectin Pour on	Closantel	Curafluke 5%	Rafoxanide
Trodax 34%	Nitroxynil	Curafluke 10%	Rafoxanide
Deldrax 34%	Nitroxynil	Panafluke Oral Suspension	Rafoxanide
Flukinex 9%	Rafoxanide	Fasinex 24%	Triclabendazole
Orafluke 5%	Rafoxanide	Endex 19.5%	Triclabendazole
Orafluke 10%	Rafoxanide	Fasinex 10%	Triclabendazole
Fluken worm	Rafoxanide	Fasinex Super 19.5%	Triclabendazole
Levafluke	Rafoxanide		
Triazole	Rafoxanide		
Fenafluke 5%	Rafoxanide	Triclaben 10% for cattle	Triclabendazole
Chan Broad Spec	Rafoxanide	Tribex 10% for cattle	Triclabendazole

Closantel: subcutaneous administration using 10 mL of Flukiver 50 mg mL^{-1} per 100 kg live weight
Milk collected regularly and analysed for residue



Migration of residues to product



Results

Nitroxinal levels in the milk decreased during the experimental period

All the Nitroxynil was recovered during the separating process between skim and cream

Between 95% and 98% of the Nitroxynil migrated from whole to skim milk. The remainder was within the cream

When skim milk was converted to skim milk powder, almost 100% of Nitroxynil was transferred into the powder, despite the high temperatures used during the manufacturing process

Thus it is critical that similar research be conducted for other active ingredients in animal treatment products to ensure avoidance of risk to public health

Summary

- Flukicide treatment is not suitable during lactation as the withdrawal periods are too long. Closantel residues can still be detected in the milk after 150 days

- Treatment during the dry period is more suitable, if not done properly may result in residues

- Heat, both pasteurisation and powder manufacture does not effect the presence of the residue

- For Triclabendazole, even at undetectable residue levels in the milk, there was still a presence of the residue in certain products made from that milk

- Residues were stable during storage, some even increasing in concentration

Trichloromethane (TCM) in Lactic Butter

Problem:

- Manufactured in Ireland exported to Germany, market, residue
- Germany - legal max level of TCM:

  0.1 mg/kg product

- Suspicion – carcinogenic and liver damage
- Dairies in Germany check regularly
- Irish butter – relatively high levels TCM
- Position within the market is vulnerable

Target

German legal limit : 0.10 mg/kg

Product exported from Ireland :

0.04 – 0.1 mg/kg – approaching legal limit

Marketing tool

Target for butter : 0.03 mg/kg

Target for cream: 0.015 mg/kg

Target for milk : <0.002 mg/kg

Development of TCM

TCM arises from cleaning and disinfecting procedures involving chlorine containing solvents

Normal to use chlorine compounds - most effective and economical antimicrobial - >90%

Active chlorine contact with an organic material, forms total organic chlorine

Incorporates volatile organic chlorine - TCM

TCM develops within the solvent

Used and often re-used – develops further

If this solvent is not removed by rinsing, then, TCM will be transferred to the milk

Critical points for TCM

Rinsing of milking plant after milking and pre-detergent cycle

Correct use of chlorine detergent (supplier)

Re-use of chlorine detergent solution

Rinsing post-detergent cycle

Use of chlorine in cluster dipping procedure

Recommended approach for milk processors

Remove chlorine out of manufacturing process

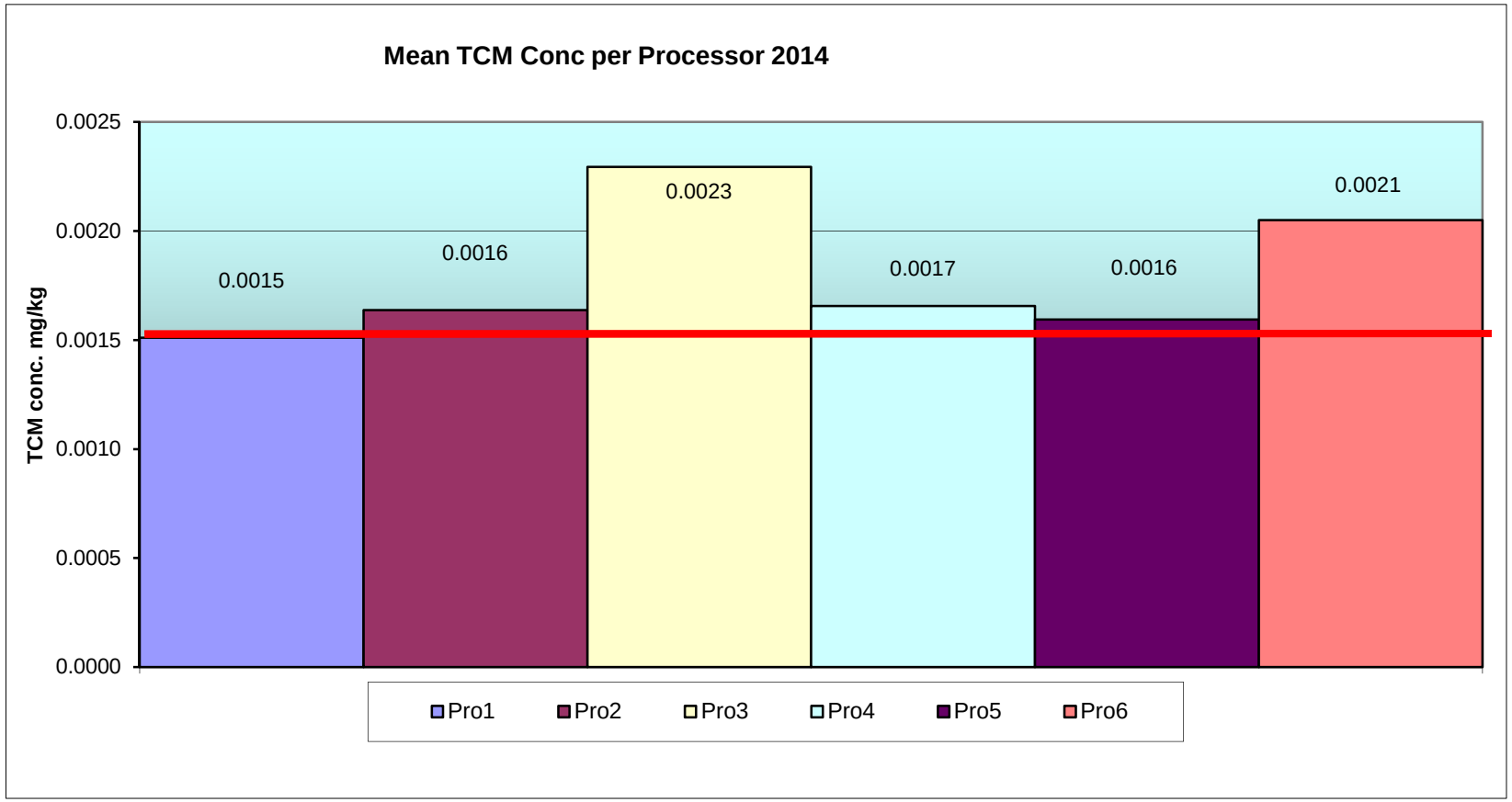
Train personnel washing tankers / silos /vats

Initiate communication with farmers on correct washing procedures

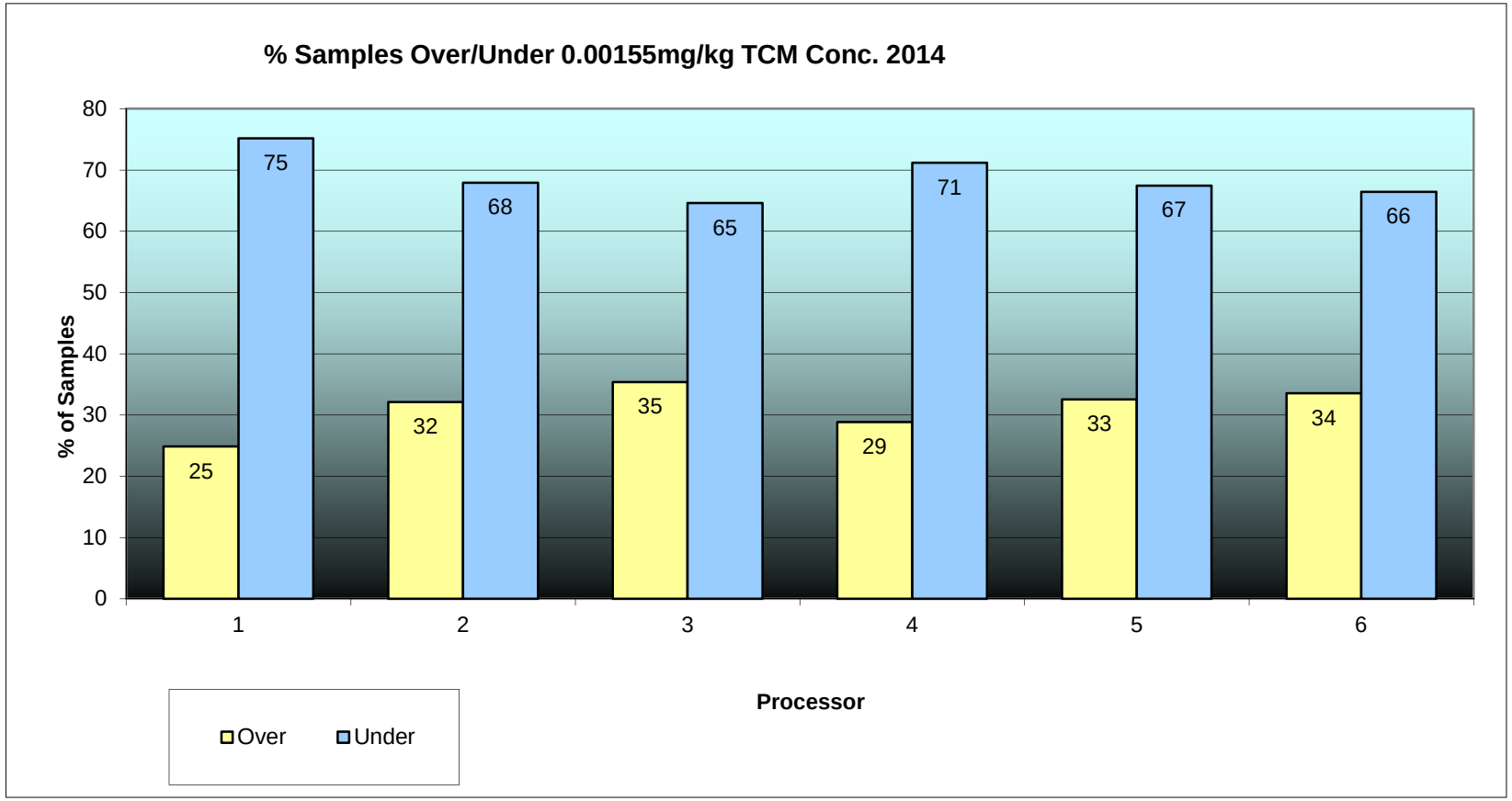
Commence sampling at tanker level to identify scale and location of problem (select appropriate routes and numbers that can be dealt with)

Can then identify individual farms that have TCM problem – individual advisor attention is required on those farms

Results – mean TCM values (approx 25,000 samples /year)



Results - % over/under the limit



IDB

TCM mtg July 2015 IDB.pdf

Quaternary Ammonium Compounds

Industrial biocides - minimize bacterial growth and biofilms

Present in, e.g. teat sanitizing wipes; new teat dips (new project)

EU member states required to carry out investigations

DEHP - one of a number of phthalate products

- **Up to 100 different phthalates in commercial use**
- **More than 90% of phthalates produced in Europe are used to plasticize PVC (polyvinyl chloride) to make flexible PVC products**
- Di ethylhexyl phthalate is a cost effective general purpose plasticiser mainly used to make PVC soft
- R**egulations - National legislation in France, Netherlands, Czech republic**
- **Danish ban on DEHP, DBP, DIBP and BBP came into force 2013**
- **No specific measure at national level in Ireland**
- **Processors obliged to make sure all food contact materials comply-DECLARATION OF COMPLIANCE- Migration**

- DEHP is subject to authorization under REACH which means it can no longer be used in the EU after the 21 February 2015, in any production processes, unless authorization has been granted.
- Authorization is granted to a particular manufacturer and their particular chain of downstream users, for specific uses only
- Reg - migration of phthalates into food
- Based on different conditions of use and contact with food practise, rubber articles are divided into 4 categories
  - Prolonged contact
  - Medium contact
  - Short contact – milk liners, milk tubes
  - Insignificant contact

Migration

- **DEHP allowed for short term contact products such as liners, seals, tubing, conveyer belts**
- **Max migration allowed - 10% DEHP migration of total weight**

- Public Analysis Laboratories, Dublin
- **Migration tests for plastic surfaces only, not interested to applying the test to rubber products**
- Eurofins:
  - **Rubber @ 237 x vat, multiple samples @190**
  - **Milk @ 180 x vat, multiple samples @ 150**
- **Accredited test- lab Germany, 8 working days**
- **Analytical laboratories Birmingham • £73 per sample- 5 working days,**
- **National Food & envir. res. agency, York - • 570 per sample, minimum of 5 samples**

New Project 2015

Task Title:

Potential sources and factors influencing phthalate residue levels in bulk tank milk in Ireland

Start date 01/01/15

Objective: To establish the sources of Phthalate residues in Irish bulk tank milk and to give guidelines to industry on minimizing potential routes of entry.

Initial step to establish levels of DEHP on rubber used on farms

- **Steps:**

1. Establish laboratory using accredited tests to establish the presence & levels of DEHP in rubber

2. Submit 8 milk liners for analysis- Milk-rite UK; Skellerup NZ; Westsfalia, Germany; Buomatic, US

3. In samples where DEHP is observed- conduct migration analysis measurements

Chlorates

Chlorate

- Chlorate is formed as a by-product when using chlorine, chlorine dioxide or hypochlorite for the disinfection of drinking water, water for food production and surfaces coming into contact with food.
- Chlorate formed during the slow decomposition of sodium hypochlorite solutions (Adam et al., 1992; Hutchison et al., 1994).
- The concentration of chlorate increases during storage as a function of time, temperature
- Currently, there is no known treatment available to remove chlorate ion once it has been formed in drinking-water

Chlorate

- No specific maximum residue levels (MRLs) have been established for chlorate under Regulation (EC) No 396/2005
- A default MRL of 0.01 mg/kg is applicable
- Only recent developments allowed analysis of chlorate to levels of µg/kg range
- Subsequently, chlorate analysis has been included in screening programmes and was found in samples at concentrations up to several mg/kg - veg
- Methodology involves LC coupled with MS
- Indications that high levels of chlorate might be present in yoghurt and infant/follow-on formula but the data were insufficient for exposure assessment
- Affects red blood cells and can inhibit thyroid iodine uptake

Study of Asami et al. 2009

- Water can be most important source of chlorate
- Scientific journal “Science of the total environment” 2009
- The contributions of water to total levels of chlorate intake were determined using food and water samples from 10 locations in Japan between 2008 and 2009. Foods were categorized into 13 groups and analyzed along with tap water. The average total chlorate intake was 333 µg/day for samples cooked with tap water

The contribution of tap water to total chlorate intake was 47%–58%, although total chlorate intake was less than 32% of the tolerable daily intake, 30 µg/day per kg body weight

Recommended to gather more information about the impact of food processing on chlorate residues in food. More occurrence data are needed for foods for which there are currently no data (e.g. animal derived foods, tea, coffee, beer)

Any efforts to reduce chlorate residues in food should take into account whether these would have an impact on microbiological food safety

Sodium hypochlorite

Characteristics:

- easily be stored and transported
- dosage is easy
- safe and effective product for disinfection
- BUT sodium hypochlorite solutions contain many regulated and unregulated contaminants including bromate and chlorate (Asami et al, 2009; Greiner et al, 2008; Weinberg et al, 2003; Gordon et al, 1993).

Recommendations

A quick solution to maintain low chlorate levels :

- A quick turnover of sodium hypochlorite storage
- Frequent cleaning of the storage tank can prevent old sodium hypochlorite from remaining in the tank
- Temperature reduction and/or dilution of the solution on receipt from the supplier can also reduce the formation of chlorate
- Store hypochlorite solutions at a lower temperature - every 5o C reduction in storage temperature will reduce the rate of chlorate formation
- Control the pH of stored hypochlorite solutions at a pH of 11-13 even after dilution

Recommendations cont.

- Dilute stored hypochlorite solutions on delivery since the decomposition of hypochlorite and subsequent formation of chlorate is dependent on hypochlorite concentration and ionic strength. A higher ionic strength and hypochlorite concentration will lead to greater production of chlorate

- For example: diluting a 2 molar hypochlorite solution by a factor of 2, the rate of perchlorate formation decreases by a factor of 7; a four-fold dilution will decrease the rate of formation by factor of 36;
- Fresh hypochlorite solution should be used when possible.

Analysis

- Ashtown, Eurofins
- Cost of samples 145€ / sample
- 50-100g milk
- LC+MS method
- Detection level = 0.01 mg/kg
- 15 samples (5 high + 5 low + 5 med in TCM)
- If high TCM farms have high chlorate levels – examine use of sodium hypochlorite on high farms – and test samples NaOCl soln?


Thank you