AGRICULTURE AND FOOD DEVELOPMENT AUTHORITY

The Irish Agriculture and Food Development Authority

Veterinary Drugs to Control Liver Fluke and their fate in milk and milk products.

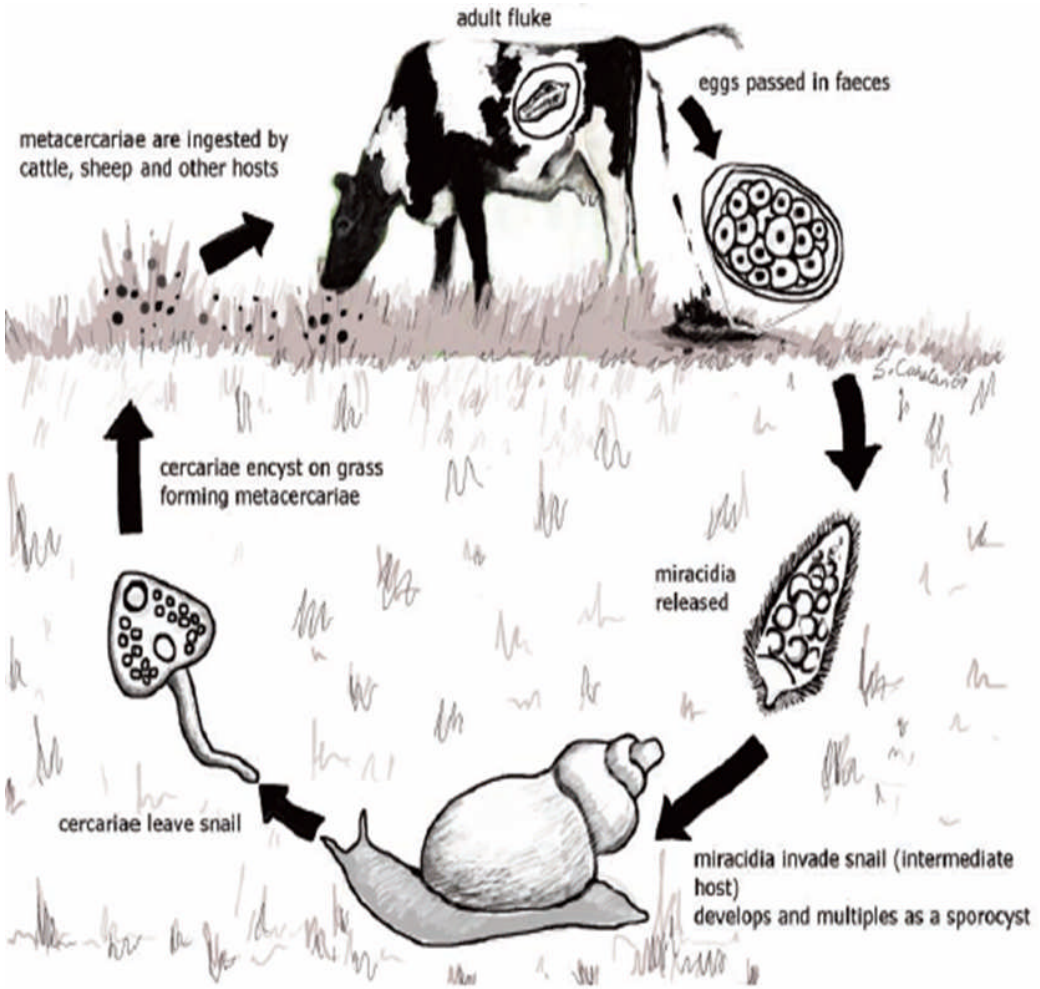
C. Power[1,5], M. Danaher[2], R. Sayers[3], B. O'Brien[4], A. Furey[5], K. Jordan[1]

[1]Food Safety Department, Teagasc Food Research Centre, Fermoy, Co. Cork, Ireland
[2]Food Safety Department, Teagasc Food Research Centre, Ashtown, Dublin 15, Ireland
[3]Animal and Bioscience Research Department, Animal and Grassland Research and Innovation Centre, Teagasc, Moorepark, Fermoy, Co. Cork, Ireland.
[4]Livestock Systems Department, Animal and Grassland Research and Innovation Centre, Teagasc, Moorepark, Fermoy, Co. Cork, Ireland.
[5]Team Elucidate, Department of Chemistry, Cork Institute of Technology, Bishopstown, Cork, Ireland

teagasc
Agriculture and Food Development Authority

The Irish Agriculture and Food Development Authority

Fluke Life Cycle



- Adults in final host
- Eggs shed onto pasture
- Larval stage
- Snail intermediate host
- Metacercariae
- Ingested by cow
- Migration
- Mature adults

Aim of Research

In licensed live trials the aim of the research was 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

Administration of flukicides to lactating cows

- Triclabendazole oral administration using 12 mL of Fasinex 10% per 100 kg
- Closantel subcutaneous administration using 10 mL of Flukiver 50 mg mL^{-1} per 100 kg live weight
- Rafoxanide oral administration using 11.75 mL of Curafluke 10% Oral Drench per 100 kg live weight.

Legislation

EU No 37/2010

Regulation on pharmacologically active substances and their classification regarding Maximum Residue Limits (MRL) in foodstuffs of animal origin

MRL in milk for flukicides

Following a scientific review by the European Medicinal Agency, Committee on Veterinary Medicinal Products (CVMP) set provisional MRL's for some veterinary drug residues in milk as follows:

- Triclabendazole 10 µg/kg (Provisional until 2014)
- Closantel 45 µg/kg (Provisional until 2014)

Note:

No provisional MRL has been set for Rafoxanide in milk

Licences for live trials

- Dept. of Health Licence under the Cruelty to Animals Act 1876 which permits the conduction of live animal experiments
- Dept. of Agriculture Licence required for each trial under the EU (Animal Remedies) (No. 2) Regulations 2007 – S.I. No 786 of 2007
- From January 1st 2013, the Irish Medicines Board (IMB) became the competent authority responsible for the implementation of EU 2010/63 on the protection of animals used for scientific purposes in accordance with the requirements of SI No 543:2012

Methodology and Results

The methodology of this research occured in two parts:

Milk: Drug administered to 6 animals during lactation and milk samples taken for each cow until residue was no longer detected
Additionally, closantel administered in dry-period

Product: Pooled milk from the above cows used to make raw and pasteurised product where the residue presence and stability was analysed

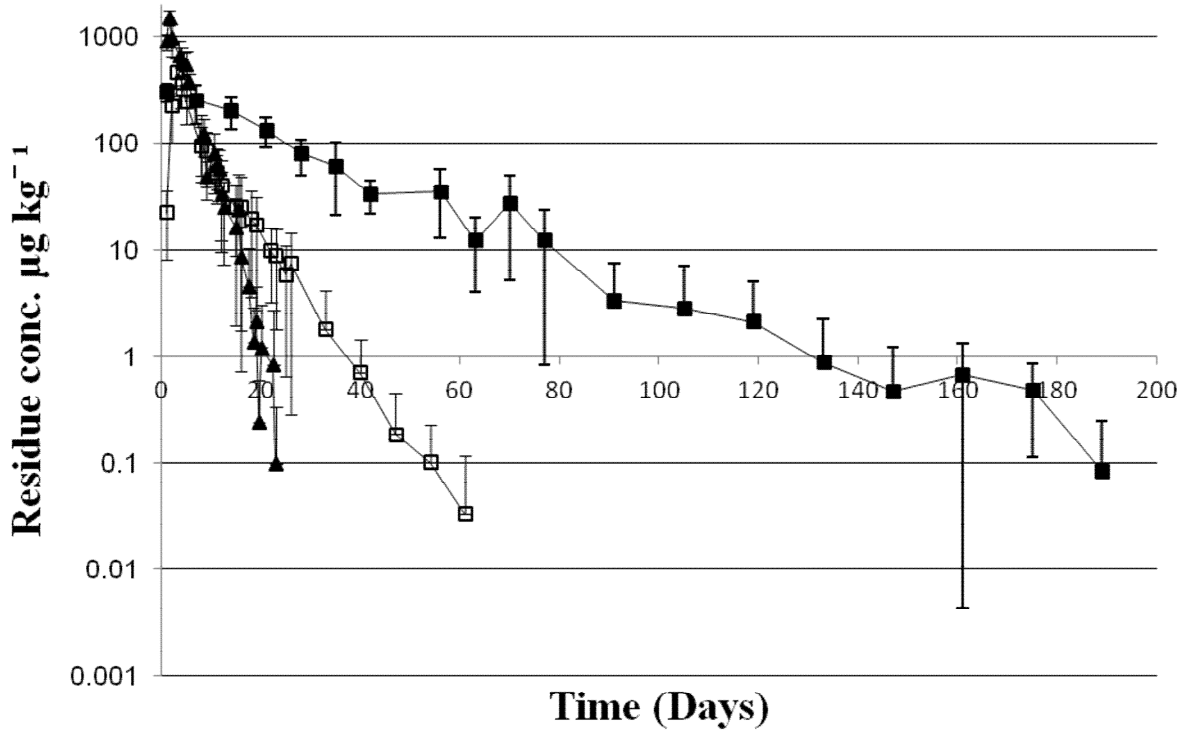
Analysis of Residues using UHPLC-MS/MS

- Sample extraction for the detection of each analyte was conducted using a QuEChERS (quick, easy, cheap, effective, rugged and safe) methods developed by Kinsella et al., (2009) and Whelan et al., (2010).The method was validated in bovine milk and liver according to the requirements of 2002/657/EC

- This method was further validated for ovine milk, caprine milk, butter, cheese and skim milk powder by Power et al., (2013a,b,c) according to the requirements of 2002/657/EC

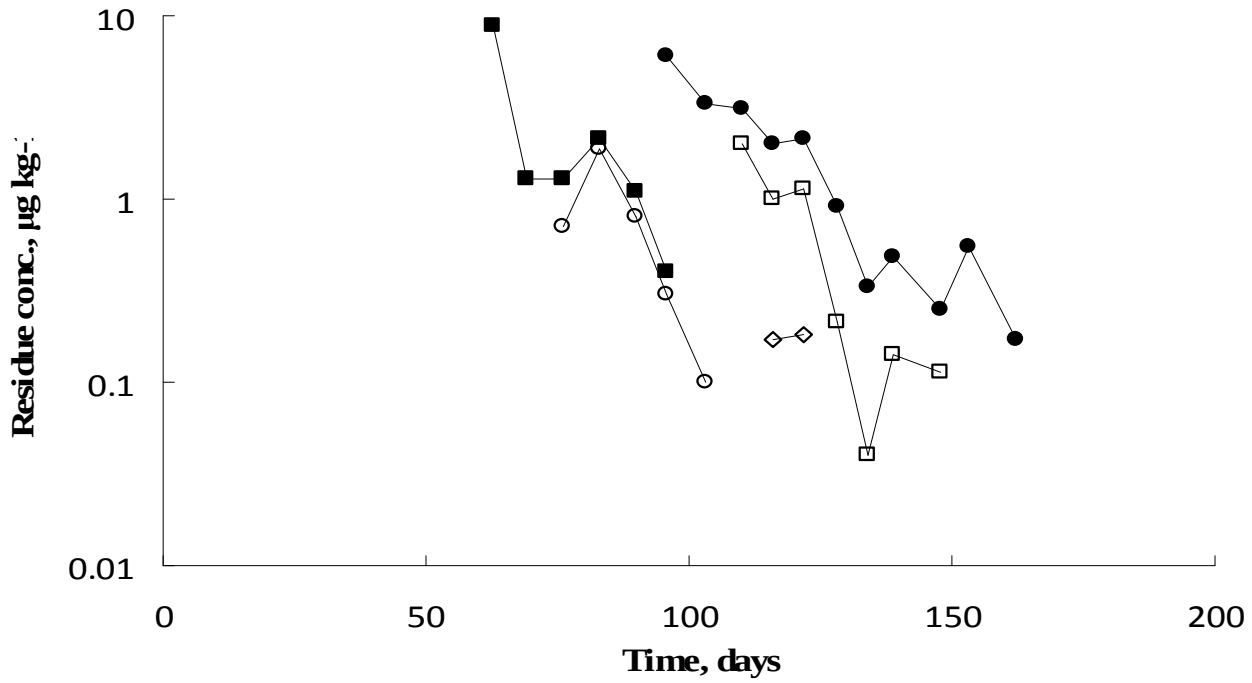
- The instrument used for analytical detection was UHPLC-MS/MS (Ultra High Performance Liquid Chromatography, Tandem Mass Spectrometry)

Depletion of flukicides in milk



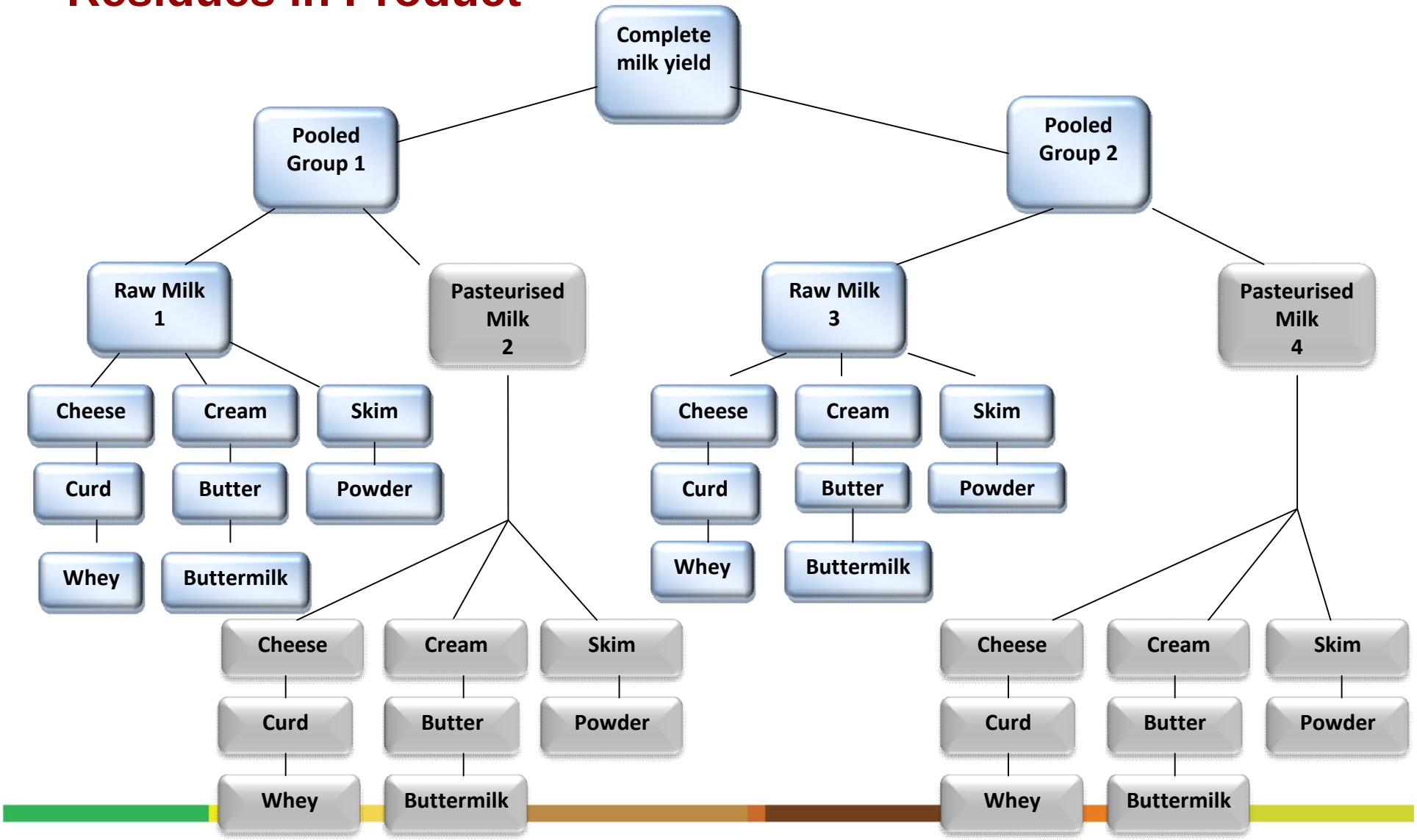
Withdrawal period for triclabendazole (▲), closantel (■) and rafoxanide (□) in milk of cows (n=6) administered each analyte

Excretion of Closantel following administration in the drying off period



Excretion of closantel (µg kg^{-1}) into milk as a function of time (days) post-calving, following administration of closantel at drying-off. The analysis of the milk from each individual cow is shown; Cow # 3429 (□), Cow # 2644 (◊), Cow # 4422 (●), Cow # 4686 (■), Cow # 4670 (○). Cow # 4584 had no detectable residue in the milk post-calving.

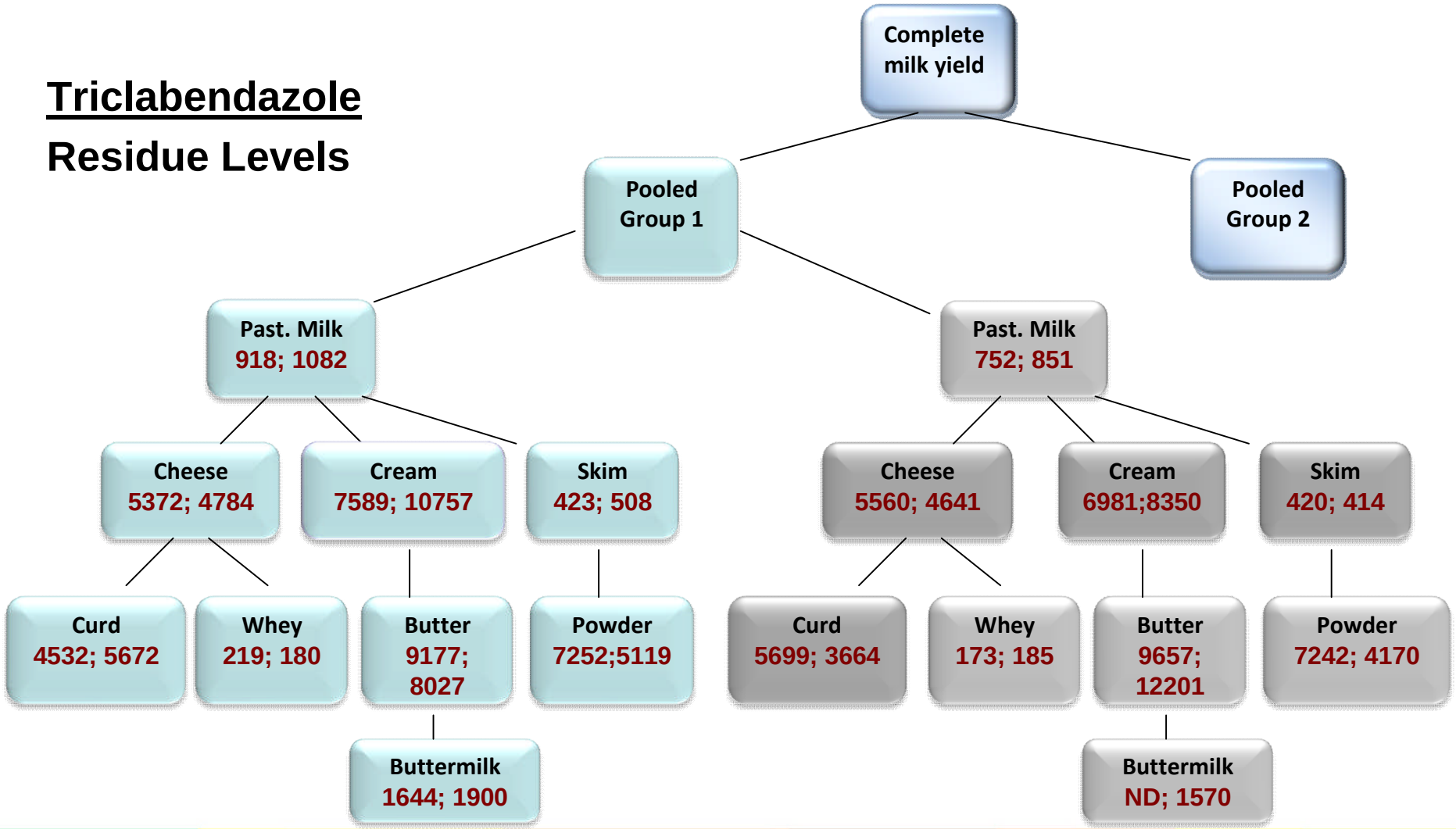
Residues in Product



Residues in Product

Triclabendazole

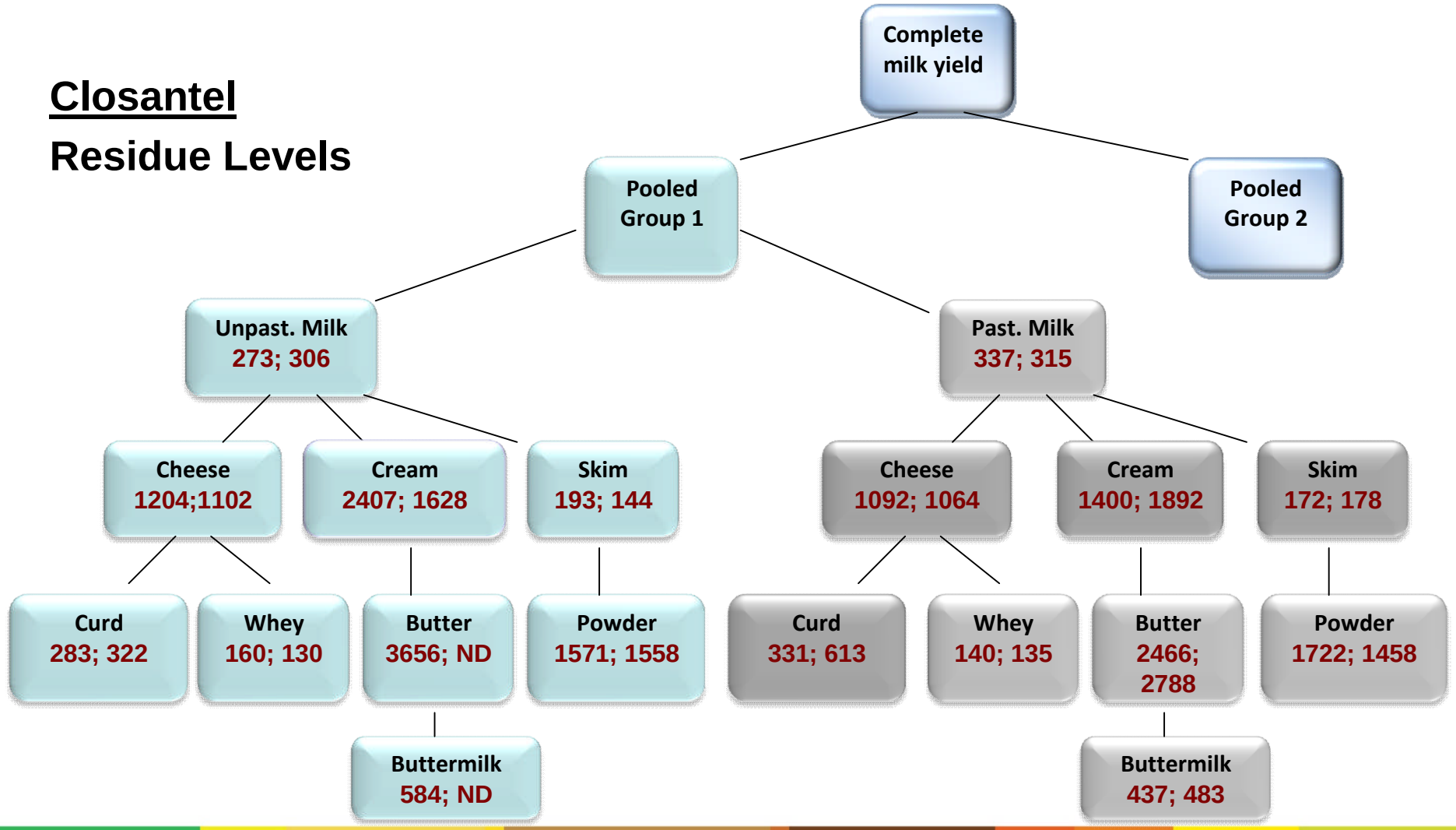
Residue Levels



Residues in Product

Closantel

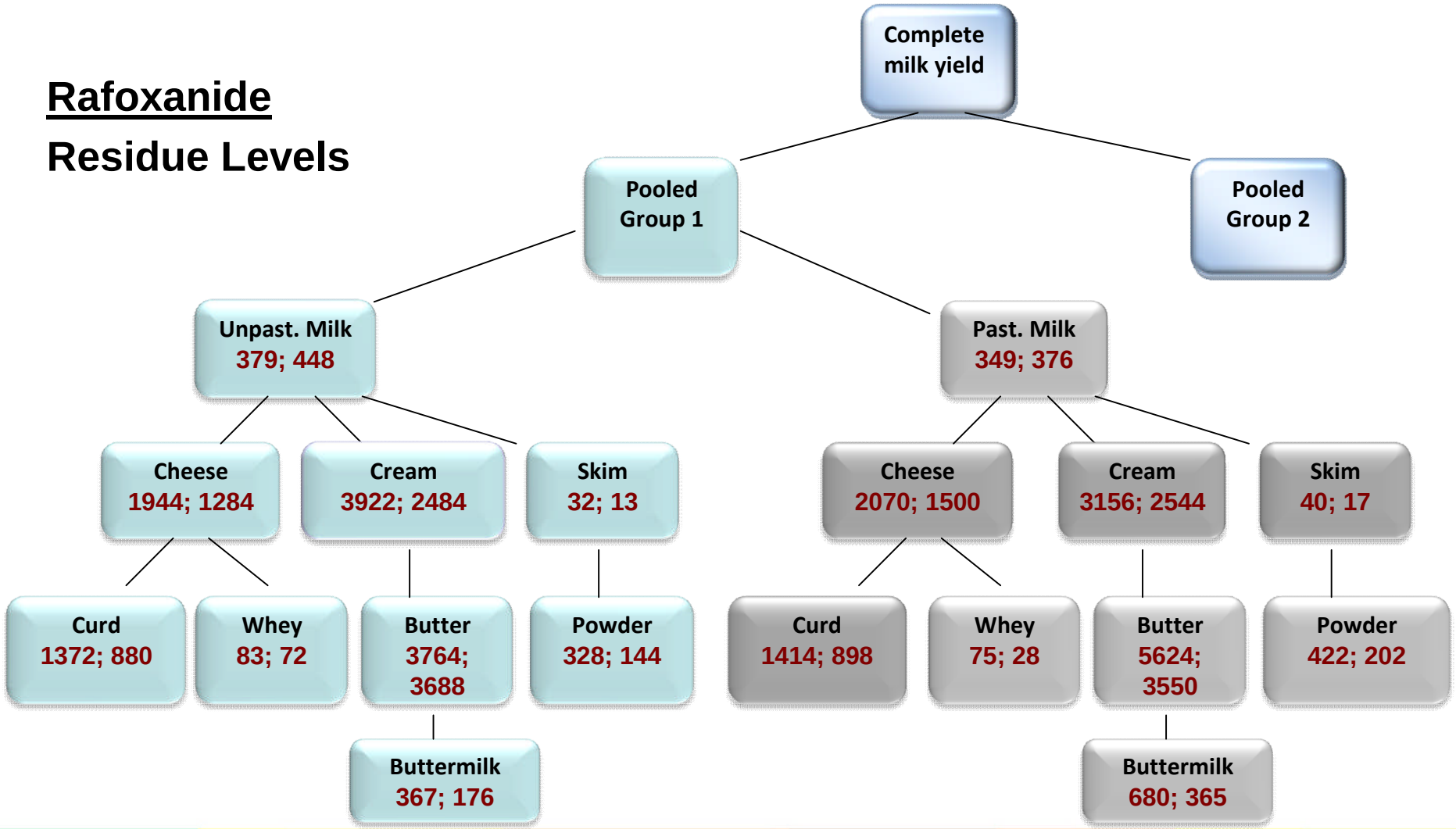
Residue Levels



Residues in Product

Rafoxanide

Residue Levels



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

Acknowledgements

- Teagasc Walsh Fellowship Fund
- Staff at Teagasc Ashtown, specifically Dr. Michelle Whelan and Martin McCormack for their technical expertise with Anthelmintic analysis
- Mr. Noel Byrne and Mr. John Paul Murphy
- Farm Staff