Lactose derivatives: turning waste into functional foods

Introduction
While cheese production steadily increases and discharge of permeate solids to effluent treatment is increasingly accepted as wasteful, dairy manufacturers face a choice of seven options to utilise their permeate streams from milk and whey (sweet and acid) drying, fermentation into various products (ethanol, lactic acid, bacteriocins), lactose production, protein standardisation of milk powders (with milk permeate or lactose derived from whey permeate), lactose hydrolysis, recovery of minor components and synthesis of derivatives from a lactose-rich feedstock. As whey permeate is currently underutilised (Gänzle et al. 2008), significant research and development focus on permeate and lactose-derived ingredients (galacto-oligosaccharides, lactulose, lactosucrose, lactitol, lactobionic acid, tagatose and sialyllactose). Many oligosaccharides are already on the market, lactulose is an established pharmaceutical product, and commodities such as lactose and permeate powder still make up the most significant part of the lactose business (Afferstohl-Allen 2007). However, high value-added lactose derivatives ($5000/t to $10,000/t) are showing interesting new application opportunities and significant annual growth rates (5 to 20%). The objective of this review is to highlight recent research related to the manufacture or the applications of the lactose derived prebiotics as well as other derivatives attracting increasing interest because of their various health and functional benefits. As noted by Peters (2005), the identification of the different avenues for permeate utilisation is important because future sustainable economic gains from whey products will most likely be built on the lactose derivatives rather than the protein streams.

Prebiotics
According to the updated concept of Gibson et al. (2004), prebiotics are selectively fermented ingredients that allow specific changes, both in the composition and/or activity in the gastrointestinal microflora that confer benefits upon host wellbeing and health. The main applications for prebiotics currently are in infant, clinical and geriatric nutrition and in food segments such as beverages, dairy products (yogurts especially) and bakery products, although they could potentially be incorporated in many other food products for both human and animal consumption (Crittenden and Playne 1996; Gibson et al. 2004). Two out of the three carbohydrates which completely fulfill the criteria for prebiotic classification are lactose derivatives (galacto-oligosaccharides and lactulose), the third one being the main fructo-oligosaccharides (Goulas et al. 2007). A larger variety of ingredients are produced and marketed worldwide as prebiotics; they are already accepted by consumers but convincing scientific evidence about their non-digestibility, fermentation and activity is still lacking, as is the case for lactosucrose (Gibson et al. 2004). The properties and applications of the main commercial prebiotics are presented in Table 1.

Abstract
Whey permeate-derived ingredients such as galacto-oligosaccharides, lactulose, lactosucrose, lactitol, lactobionic acid, tagatose and sialyllactose have been the focus of intense research investigating their health and functional properties for the past 20 years. Despite the research, those derivatives are not always considered by dairy manufacturers to carry enough added value to alter the focus on commodities such as permeate powder and edible grade lactose which still represent the principal outlets for permeate solids utilisation. However, the review presented in this paper summarises the recent research published in the last decade on lactose derived functional ingredients and shows that significant opportunities can arise from investing in added value ingredients issued from permeate streams, especially where market sizes are higher than 10,000 tonnes per annum and annual growth is stronger than 5%. Galacto-oligosaccharides and lactobionic acid are two examples of promising functional ingredients coming from otherwise wasted whey permeate.

Galacto-oligosaccharides
Human milk oligosaccharides (HMO) are important components of breast milk representing, at peak, 27% of the total carbohydrates in colostrum (Darragh 2003). The conviction that HMO play vital roles in the development of the human infant has coincided with a surge in research. HMO are numerous, more than 130 identified compounds, diverse with respect to saccharide residues and glycosidic bond and variable with time for an individual and between different individuals (Kunz and Rudloff 2006). Compared to HMO, galacto-oligosaccharides (GOS) synthesised from permeate and other lactose-rich streams by a transgalactosylation reaction catalysed by β-galactosidase, are usually simple mixtures of tri- and tetra-saccharides made up of glucose and galactose molecules along with residual lactose, glucose and traces of galactose. The enzyme, β-galactosidase, which normally favours hydrolysis, can be used at high temperatures and high lactose concentrations, to form a mixture of galacto-oligosaccharides. Some enzymes favour 1,4-links while others favour 1,6-links between the monosaccharide residues. As GOS composition will change with the source of the enzyme used, GOS products from different manufacturers are expected to vary. Other points of difference between products relate to their degree of purification and their
(undesirable) mineral content. GOS are available as powders or as syrups, typically with about 75% solids, of which actual oligosaccharides comprise about 55-60% (Goulas et al. 2007).

GOS are non-digestible prebiotics which promote a healthy bifidobacteria colonic microflora in humans and may protect against gut pathogens. They have been used for some time in foods in Japan where they are accepted as “foods for specified health use” (FOSHU) and were recently approved for use in infant foods by Food Standards Australia and New Zealand in 2008 (FSANZ 2008). Their main use is in infant formula but they are likely to spread to other foods with yoghurt being a likely candidate. The market price of GOS is about 10 to 12 times greater than edible lactose (Valero and Yang 2006). The current global market size is approximately 20,000 to 22,000 tonnes per annum with the fastest expected annual growth rate of all the lactose derivatives (10 to 20%) (Affertsholt-Allen 2007). While their prebiotic properties are widely accepted, GOS can also have varying health and technological benefits. They are non-carogenic, and have been found to have a positive effect on constipation and increase calcium absorption. They are half as sweet relative to sucrose and yield half the energy. They are heat and enhancing properties and function as hygroscopic, water soluble, ingredients to the food industry rather than for targeted applications. Functionally enhanced prebiotic GOS could be produced to target specific group of bacteria (Rastall and M 2002) through a better understanding of the factors determining the prebiotic activity of a particular GOS and new developments in the manufacturing processes.

**Lactulose**

Lactulose is a semi-synthetic disaccharide made from lactose by isomerisation catalysed by sodium hydroxide and being a known medicine for the treatment of specific medical conditions (constipation, chronic hepatic encephalopathy) and as a prebiotic (at that time named ‘bifidus factor’), although the nomenclature of pre- and probiotics has only come into use much later. For this reason lactulose became known to science first as a medical drug but has become increasingly important for the food industry as a prebiotic. Lactulose is classed both as a prescription and non-prescription drug depending on the country. However, in Italy, Japan, and the Netherlands, lactulose can be sold over the counter. In the food industry, it is mainly used as a medical food ingredient (Kitaguchi et al. 2007) and in infant formula (Vasiljevic and Jelen 2009).

**Table 1: Properties and applications of lactose derivatives commercially used as prebiotics.**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reducing sugar</th>
<th>Maillard Browning</th>
<th>Relative sweetness</th>
<th>Prebiotic status</th>
<th>Other claimed health benefits</th>
<th>Potential segments</th>
<th>Manufacturers</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOS Domo;</td>
<td>yes</td>
<td>yes</td>
<td>0.3 – 0.6</td>
<td>yes</td>
<td>Protective against bowel cancer and constipation; Anticaries; Calcium absorption in gut Low energy</td>
<td>Infant formula; Beverages; Yogurts and dairy products; Bakery products; Sweeteners</td>
<td>Friesland Foods</td>
</tr>
<tr>
<td>Ingredients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactulose</td>
<td>yes</td>
<td>yes</td>
<td>0.6</td>
<td>yes</td>
<td>Laxative; Chronnic hepatic encephalopathy; Reduced symptoms in inflammatory bowel disease; Increased antibiotics efficacy; Mineral absorption; Low energy Anticaries; Calcium absorption in gut</td>
<td>Medical uses; Diabetic food; Soft drinks and beverages; Infant formula; Yogurts; Pet food</td>
<td></td>
</tr>
<tr>
<td>Lactosucrose</td>
<td>no</td>
<td>no</td>
<td>0.3 – 0.6</td>
<td>More data needed</td>
<td>Sweeteners; Dairy products; Beverages</td>
<td></td>
<td>Hayashibara; Ensuiko</td>
</tr>
</tbody>
</table>
Lactitol is produced from the catalytic hydrogenation of lactose to produce the sugar alcohol. There are several recent patents describing the manufacture of crystalline lactitol (Heikkila et al. 1998; Heikkila and Nurmi 2003; Myers et al. 2005). Lactitol is used as a low calorie sweetener and as a laxative, it also acts as a dietary fibre, competing against sorbitol and maltitol. Not absorbed through the small intestine, lactitol does not raise blood glucose levels and is thus suitable for diabetic foods (Drakoularakou et al. 2007). The current market is approximately 10,000 tonnes per year with an annual growth rate of 2-4% (Affertsholt-Allen 2007).

Lactobionic acid

Lactobionic acid is obtained by oxidation of lactose either by electrolysis, patents for which can be traced back to the work of Isbell and others in the 1930s, or by the enzyme hexose oxidase. Its current commercial applications are in the chemical and medicinal fields rather than in the functional foods area. The calcium chelating property of the lactobionate form is used in calcium supplements in pharmaceuticals and as an ion sequestrant in detergent solutions. Lactobionic acid is also used in the formulation of solutions for the cold storage transport of transplant organs. The current market size for lactobionic acid is approximately 15,000 to 17,000 tonnes per year and is expected to have an annual growth rate of 5% (Affertsholt-Allen 2007).

Two areas of research on lactobionic acid can be outlined from the literature. The first one focuses on achieving a beneficial change, such as acidification, in the food itself. The second one looks at the formation of lactobionic acid with a view to using it for use as a food ingredient either in the acid form or as a calcium salt. Many patents have been granted in the last ten years for isolation and use of hexose oxidase primarily for cross-linking proteins and/or phenolic groups in bread and biscuit doughs to achieve textural advantages in baked goods. Inevitably, the commercial availability of this enzyme has rekindled interest in its dairy applications explored 35 years ago by Rand (1972) for the enzymic acidification of milk to augment or accelerate

### Table 2: Properties, health-related benefits and applications of non-prebiotic lactose derivatives.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Relative sweetness</th>
<th>Prebiotic status</th>
<th>Other claimed health benefits</th>
<th>Potential segments</th>
<th>Manufacturers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactitol</td>
<td>0.3</td>
<td>More data needed</td>
<td>Prevention of constipation; Low energy</td>
<td>Sweeteners; Laxative; Diabetic foods</td>
<td>Danisco; Purac;</td>
</tr>
<tr>
<td>Lactobionic acid sour</td>
<td>More data needed</td>
<td>Cold storage of transplanted organs; Calcium fortification</td>
<td>Detergent and chemicals (calcium chelator, ion sequestrant); Dairy products (acidulant)</td>
<td>Infant formula</td>
<td>Towa; Nikken; Solvay; Sandoz; US Dairy Ingredient Co., Friesland Foods</td>
</tr>
<tr>
<td>Syrallylactose</td>
<td>0.2 – 0.6</td>
<td>no</td>
<td>Cell adhesion; Protection against pathogenic attacks</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Hydrolysed lactose</td>
<td>0.6 – 0.9</td>
<td>no</td>
<td>Alleviation of lactose malabsorption</td>
<td>Lactose-hydrolysed dairy products, whey drinks; Feedstock for other transformations; Pet food; Concentrated dairy products (lactose crystallisation control)</td>
<td>Valio; Others</td>
</tr>
</tbody>
</table>
acidification by micro-organisms as in yoghurt or cheese. Recent patent activity has focused on the use of the enzyme for synthesis of lactobionic acid which is of interest as a food acidulant and, in the form of the calcium salt, for calcium fortification.

**Sialylactose**

Sialylactose is recovered directly from whey permeate rather than being derived from lactose however its potential health benefit particularly cell adhesion, from both beneficial and pathogenic bacteria, and derivatives (Peters 2005). Research has already uncovered the unique functional properties and some of the processes to deliver those good returns on the market stage lies in using lactose rather than edible grade lactose as a gateway for product stream consistency. A purified lactose stream would bring greater flexibility to the ways in which manufacturers can use the lactose in whey permeate whether it be in protein standardisation or other established uses, or liquid lactose or higher value lacto derivatives. Two good candidates identified by this review are presenting sizable markets with high value and annual growth rates above 5% would be galacto-oligosaccharides and lacto-biose.

**Hydrolysed lactose**

Lactose can be enzymically hydrolysed into glucose and galactose with β-galactosidase, producing a syrup which is more easily digested by those who are lactose intolerant. Many lactose-hydrolysed milks, milk powders and yoghurts are available around the world. Lactose intolerance has been reviewed by Savaiano's group (Hertzler et al. 1996; Savaiano et al. 2006). Hydrolysed lactose is sweeter and more soluble than lactose and can be used for sweetening syrups in ice creams, yoghurts and drinks without lactose crystallisation problems. Lactose-reduced milk products are commercially produced either by adding β-galactosidase directly into the product or by immobilisation of the enzyme on a resinsuch as the HYLA range produced by the Finnish company Neose. Sialylactose is recovered directly from whey permeate rather than being derived from lactose however its potential health benefit particularly cell adhesion, from both beneficial and pathogenic bacteria, and derivatives (Peters 2005). Research has already uncovered the unique functional properties and some of the processes to deliver those good returns on the market stage lies in using lactose rather than edible grade lactose as a gateway for product stream consistency. A purified lactose stream would bring greater flexibility to the ways in which manufacturers can use the lactose in whey permeate whether it be in protein standardisation or other established uses, or liquid lactose or higher value lacto derivatives. Two good candidates identified by this review are presenting sizable markets with high value and annual growth rates above 5% would be galacto-oligosaccharides and lacto-biose.

**References**

Mantavors, F., Formari, T. and Martín-Alvarez, P.J. (2007), Selective fractionation of saccharide mixtures by supercritical CO₂ with ethanol as co-solvent. J. Supercritical Fluids 41 (1), 61-67.