Noumi Limited Submission
FSANZ Call for Submissions - Application A1253

9 October 2022. 216-22

Bovine Lactoferrin in infant formula products

Executive summary

Synlait (**The Applicant**), a NZ based Lactoferrin producer, has applied to FSANZ to have Lactoferrin (**a dairy milk whey protein**) included in the food standards code as a 'nutritive substance' in infant formula products. Lactoferrin is an iron-binding protein that is naturally present in the human body and is also found at high levels in human milk (1230-3390 mg/L), at lower levels in bovine milk (140-200 mg/L: Noumi Limited milk monitoring data) and in infant formula products not fortified with Lactoferrin (~15 mg/L). The Applicant is also seeking a 15-month exclusive use of Lactoferrin in infant formula products, the rationale for which is unjustified.

Infant formula products are highly regulated, which is prudent given such products are consumed by the most vulnerable of consumers. Thus, Noumi Limited, an ASX listed manufacturer of premium PUREnFERRIN® Lactoferrin in Shepparton (Victoria, Australia) (**The Submitter**) welcomes clarification in law as it relates to Lactoferrin quantities which can be added safely to infant formula products. However, Noumi believes Lactoferrin should be categorised a '**traditional food**' ingredient and not a '**nutritive substance**' when added to infant formula, given its long history of safe consumption by babies from breast milk ingestion and via infant formula intake in other jurisdictions around the world and because the homology between human and bovine lactoferrin is high at ~70%.

If Application A1253 is successful, it will have significant commercial consequences for the Lactoferrin producing industry in Victoria, because a listing of Lactoferrin as a 'nutritive substance' in infant formula could result in Lactoferrin being prohibited from addition as a food ingredient to any other food product. This will prevent launching and commercialising Lactoferrin containing food products for domestic purposes, which Noumi has been researching and developing over the last 18-24 months. This could ultimately impact jobs and ongoing new food product development and attenuate resulting forecast profit growth for Australian Lactoferrin producing companies.

Importantly, Noumi's argument is that Lactoferrin is **not** added to food as a nutritive substance but is instead added to achieve a '**health effect**', like immune health effects, gut health or skin health support, according to the clear definition of health effects outlined in Standard 1.1.2 of the Food Standards Code. In fact, in the FSANZ Call for Submissions to Application A1253, FSANZ stated that Lactoferrin is included in products for its '**health effects**'.

noumi
Imagining a healthier tomorrow

Noumi Limited Background

Noumi Limited is a leading Australian manufacturer of **premium dairy protein ingredients like its branded PUREnFERRIN® Lactoferrin** and shelf-stable dairy and plant-based beverages and supplementary foods. Noumi is driven by its purpose of 'Imagining a Healthier Tomorrow'. From its pioneering origins in plant and dairy beverages to its expertise in premium dairy protein ingredients, Noumi blends the wonders of natural dairy milk and plant ingredients with the power of science to nourish its consumers, communities, and our planet. Formerly Freedom Foods Ltd, Noumi represents a new era of growth and opportunity, with a clear path and direction to shape a bright future and nourish its thriving communities.

Noumi products are organised into three major product groups. The first is Noumi's PURE premium dairy protein business, where Noumi's premium **PUREnFERRIN® Lactoferrin**, PUREnWHEY® and PUREnMCC® protein ingredients are derived directly from filtered fresh cow's milk and not cheese derived. The second is Noumi's strong dairy and plant-based beverage product portfolio, to deliver on Noumi's promise of positive nutrition for a healthier tomorrow. The third stream is supplemental and specialised nutrition (added value) dairy and plant food and beverages, to meet the nutrition needs of specific consumer groups across the lifespan. A fourth product stream is Noumi's basic dairy components ingredients business, for business-to-business customers.

Noumi's PUREnFERRIN® Lactoferrin production process summary

Noumi's PUREnFERRIN® Lactoferrin is, like The Applicant's Lactoferrin, extracted directly from raw dairy milk and is not a by-product of cheese making. PUREnFERRIN® is then concentrated to produce a liquid concentrate before pasteurisation (Figure 1). The liquid concentrate is pasteurised by heating to a temperature and for a time effective to do so, after which the pasteurised liquid concentrate is gently spray dried under non-denaturing conditions to produce a light pink Lactoferrin powder in which substantially all the Lactoferrin is in its native (non-denatured) form (see Appendix 1 for a detailed process flow.)

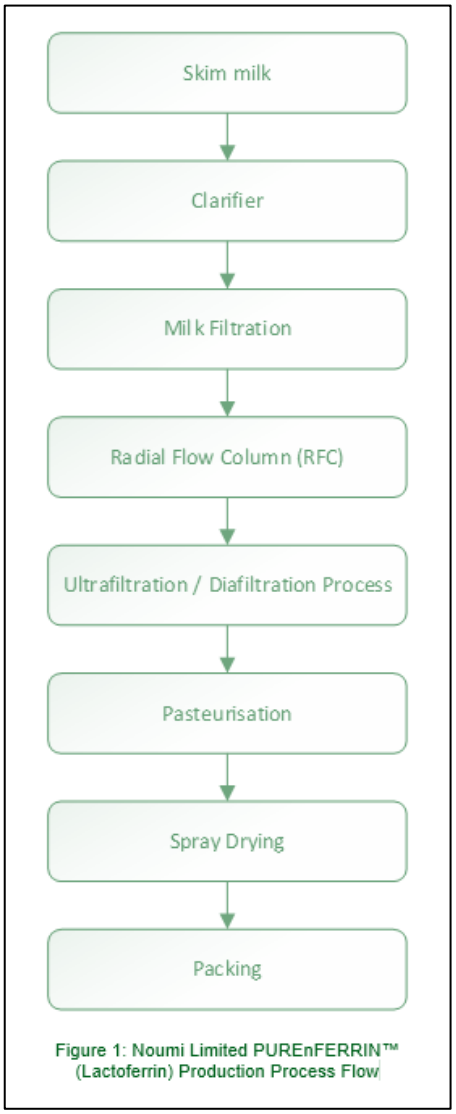

Figure 1: Noumi Limited PUREnFERRIN™ (Lactoferrin) Production Process Flow

Noumi produces around 28 metric tonne of PUREnFERRIN® Lactoferrin per year for domestic and global markets and as such, manufactures around 7% of global Lactoferrin production. This follows significant investment of more than $150M in its PUREnFERRIN® manufacturing facility over the last 5 years in its Shepparton (Victoria, Australia) processing plant.

Since 2020, Noumi has also invested heavily with some of Australia's leading tertiary research institutes (e.g., University of Newcastle and Monash University) to fund clinical trials and basic research, to obtain human clinical data to prove PUREnFERRIN® Lactoferrin's health effects on 'enhancing the immune system'. This data will support Noumi's commercialisation pathway to include PUREnFERRIN® Lactoferrin in food for its health effect to 'enhance the immune system'. Noumi has already notified FSANZ of its self-substantiated Lactoferrin health claim to 'support the immune system' in children and adults, to enable itself and Noumi customers to obtain the commercial benefit of using this health claim in food products with PUREnFERRIN® Lactoferrin.

Application A1253 does not describe a process for production of Lactoferrin significantly different from that already in use at Noumi, thus an exclusivity period seems unjustified based on The Applicant's Lactoferrin process development. Furthermore, if the request for exclusivity is approved, it will mean that

Noumi's PUREnFERRIN® Lactoferrin will be prohibited from use for the period of exclusivity, which will have commercial consequences. In addition, as there are already existing specifications for bovine Lactoferrin around the world (e.g., China, Japan and Europe), Noumi does not support the proposed Lactoferrin specification in the Code, which appears unnecessarily restrictive, especially as it relates to the iron max. content of 15mg/100g (the error of **15g** in the FSANZ Call for Submissions is noted). The general accepted criterion is <35mg/100g.

If A1253 results in the Code being amended to list bovine Lactoferrin as a nutritive substance with permission for use in infant formula products, then Lactoferrin will be prohibited from addition to any other food product in its isolated food ingredient form.

This will impose significant commercial ramifications on companies like Noumi, which have been working on their own commercialisation pathways in recent years, whereby lactoferrin has been researched and developed at significant investment for its intended use as a traditional food ingredient in food products (including infant formula products), for its **health effect**. To date, self-substantiated food-health effect relationships, established by Systematic Literature Review from three different businesses involved in the Australian dairy industry, have been notified to and published on the FSANZ website. The condition proposed of an exclusive use permission under the Synlait brand in an infant formula product for 15 months after gazettal of the draft variation (if approved) would consequently further impact the commercial losses for these companies.

1. What is a 'food', 'nutritive substance' and 'novel food'?

1.1 Food

Under ANZ laws 'food' is defined in the individual food laws maintained by each Australian State and Territory and by New Zealand, under which the Food Standard Code (the Code) is implemented. The Code itself does not define 'food'.

The definitions of food are very broad and include anything used, or represented as being for use, for human consumption, other than a therapeutic good, and includes live plants and animals, food ingredients, food additives, processing aids or anything that comes into contact with food (other than a substance 'used in preparing a living thing').

Foods may be sold provided they are 'safe' and 'suitable', as defined in the food laws.

On this basis, we suggest that bovine Lactoferrin is a safe and suitable food and may be classified as a food ingredient, sold as a food ingredient, or combined with other ingredients to form a whole food.

Most food may be sold 'as is' or 'mixed together' without reference to the Code, unless the food falls into one of the categories for which the Code expressly requires pre-approval (e.g., foods used as a nutritive substance, novel foods, food additives, processing aids, etc.).

Standard 2.5.1 – Milk sub-clause 2.5.1-4(ii) permits 'milk components' to be added to 'cows' milk' if it 'has the same whey protein to casein ratio as the original milk'. This clause is unambiguous in permitting bovine Lactoferrin, a normal whey protein milk component, to be added back to cows' milk to replace that denatured by, for example, UHT heat treatment. In addition, Schedule 10 of the Food Standards Code recognises that a variety of milk components can be added to food as food ingredients and can thereafter be labelled as **'milk solids**.' As a result, FSANZ appears to accept that isolated milk components like Lactoferrin, lactose, milk fats and other milk components may be added to food products as traditional food ingredients and not require pre-market approval as nutritive substances.

In addition, the Advisory Committee on Novel Food (ACNF) has previously issued the opinion that bovine Lactoferrin is a normal component of cows' milk at 2-20mg/100ml, and when added to dairy products at 10-100 mg/100mL or 100g, it is a Traditional Food and not a Novel Food. Similarly, the ACNF did not suggest that Lactoferrin could be a nutritive substance. Consequently, it may be concluded that Lactoferrin is a safe and "traditional food", which may be added to most foods without regulatory restriction.

Although it is not yet widely used as a food ingredient in Australia, ~20-25% of the world's production of bovine Lactoferrin is produced in Australia and the commercialisation of Lactoferrin's use as a food ingredient in non-infant formula products is growing.

There are already several products containing Lactoferrin available in Australia, including milk based Formulated Supplementary Foods for young children (Appendix 2) and foods for adults (Appendix 3). Bovine Lactoferrin is also a permitted ingredient in therapeutic goods, with no limit on its use - Therapeutic Goods (Permissible Ingredients) Determination (No. 4) 2022 (https://www.legislation.gov.au/Details/F2022L01035/Html/Volume_2).

In the FSANZ Call for Submissions, FSANZ states that lactoferrin is included in products for its health effects. Noumi agrees that lactoferrin is a traditional food ingredient which delivers a health effect or benefit (e.g., support the immune system). However, A1253 also describes lactoferrin is used to reduce the risk of respiratory tract infections. When lactoferrin is used as a food ingredient, this could reasonably support a health claim such as 'support the immune system'. However, if the intention is to make claims about the effect itself, this would constitute a claim about "alleviation of a disease", which is a therapeutic claim and not permitted on foods. The use of lactoferrin in that context must be regulated as a therapeutic good through the Therapeutic Goods Administration.

Naturally, Noumi welcomes clarification that Lactoferrin is a safe, traditional food ingredient that may be included in infant formula safely (as do many jurisdictions globally), without further regulatory amendment but it should not be classified as a nutritive substance. It is a food ingredient that may be included in milk-based foods, including infant formula, and in fact, A1253 eloquently shows no risk associated with its inclusion and consumption as a traditional food ingredient.

As a food ingredient, that is a traditional food, Lactoferrin does not require express permission to be added to dairy products like beverages, supplementary powders and drinking yoghurts. Further, as Lactoferrin is a dairy protein which is already permitted under Std 2.9.1 - Clause 6(1) to be returned to cow's milk post processing (as a whey protein), approving Lactoferrin as a nutritive substance will cause further undue and unjustified confusion to industry.

1.2 Nutritive Substance

Classification in this category relies on the food or ingredient being:

1. a substance that has been concentrated, refined, or synthesised; and
2. added to 'the food' to achieve a 'nutritional purpose'.

These principles are similar those applied to 1) food additives (added to food to achieve a technological function in the food as sold/consumed), and

2) processing aids (added to food to achieve a technological function during processing, but not in the finished food).

However, unlike the 'technological functions' associated with food additives and processing aids that are named and/or described in the Code, a 'nutritional purpose' is not defined. This leaves it open to inconsistent and occasionally 'a pick and choose' approach to interpretation by regulatory and enforcement agencies, when approval is needed in the Code for substances added for purposes other than essential nutrition (e.g., health effects – see below).

Importantly, the Code **does not** prevent the same food (e.g., Lactoferrin) or substance being added for more than one purpose, whether these are purposes requiring premarket approval (e.g., nutritive substances) or un-regulated (e.g., Lactoferrin as a traditional food ingredient, which may be added to other foods as an ingredient). Some examples include:

- Ascorbic acid and Tocopherols are regulated as both nutritive substances, when added as vitamins (C and E), and as food additives, when added as antioxidants. The key difference is that once oxidised, from use as an antioxidant, the substance cannot also be available as a vitamin, so the important difference is the purpose of addition, or the function being performed.

- Caffeine is regulated as a food additive (flavouring) at up to 145mg/kg, BUT it is not controlled when added to food for energy management purposes at <5% in a solid or semi-solid food or <1% in a liquid food. The addition of naturally occurring caffeine, for example as guarana or green tea concentrates, is also unregulated.
- Erythritol is listed as a Generally Permitted Food Additive in Schedule 19 for use as a bulking agent. However, it may also be used at higher concentrations as an unstandardised food ingredient, with no express permission in the Code, when used as a bulk sweetener for sugar replacement. Significantly, the latter use is not regulated as "Used as Nutritive Substance".
- In addition to substances listed in Schedule 18, any food and/or a food additive permitted at GMP may be used, at an appropriate concentration, as a processing aid.

Note: most purified, refined, synthesised, concentrated carbohydrates, fats and proteins (for example dietary fibre, sucrose, polyunsaturated vegetable oils or whey protein isolate) are added to foods as nutrients (macro-nutrients) but are not classed as nutritive substances despite, in some cases, making a significant contribution to the nutritional value of the food.

In the absence of a comprehensive definition of 'nutritional purpose', there is no platform for regulators to uniformly apply or not apply, other than precedents.

In addition, the definition of nutritive substance does not provide for differences in interpretation between infants and adults. Thus, if Lactoferrin is accepted as added to achieve a nutritive purpose in infant formula products, then it follows, it must also be considered by FSANZ and jurisdictional enforcement agencies as a nutritive substance in non-infant formula products. This will only lead to further confusion amongst enforcement agencies and the food industry.

In contrast, the Code clearly does not prevent a substance from being added for a different purpose, other than a 'nutritional purpose', to the same or different foods. Thus, if Lactoferrin is reclassified as "Used as a Nutritive Substance" in infant formula, it is possible that it could still also be allowed to be used in other food products for its health effect (e.g., 'to support a healthy immune system'), in the category of an unregulated food use, so long as a manufacturer has undertaken due diligence and prepared a self-substantiated evidence dossier to support this health effect, that clearly sets out the case that this is not a 'nutritional purpose'.

However, it should be anticipated that, in the absence of a comprehensive definition of 'nutritive purpose', there will always be the potential for regulatory uncertainty for both the food manufacturer and their home jurisdiction law enforcement agency based on its approval as a nutritive substance.

There are also numerous examples when the Code is inconsistent in the application of "used as a Nutritive Substance". Galactooligosaccharide and Inulin-type fructans are expressly exempted from the definition, reflecting the decision in *New South Wales Food Authority vs Nutricia* in 2007, but subsequently, 2′-fucosyllactose and lacto-N-neotetraose (i.e., human milk Galactooligo-saccharide) have both recently been listed as "used as a Nutritive Substance" for the same functional purpose in the infant formula category. The risk for Lactoferrin under Application A1253 is that its reclassification as a nutritive substance will likely introduce inconsistencies in how the Code treats Lactoferrin (e.g., Lactoferrin is a normal milk component and has been classified as a Traditional Food in the FSANZ Advisory Committee on Novel Foods as discussed above.)

The potential for regulatory uncertainty around 'nutritional purpose' is further exacerbated by the definitions of a nutrition content claim and a health effect in Standard 1.1.2.

Nutrition content claim means a claim that:

a) is about:

  i) the presence or absence of any of the following:

    a) a biologically active substance

    b) dietary fibre

f) protein

g) carbohydrate

h) fat

i) the components of any one of protein, carbohydrate, or fat…

Firstly, this definition does not preclude a concentrated food protein like Lactoferrin from being counted as part of a final food's total protein macronutrient content and therefore, contribute to the total protein fraction that meets the requirements to make a nutrition content claim. Secondly, if taken literally, this definition could be interpreted to mean that any concentrated or refined protein (e.g., whey protein), carbohydrate (e.g., table sugar) or fat (e.g., concentrated essential fats) or any component thereof, about which a nutrition content claim can be made, could also be a substance used as a nutritionally active substance.

Health effect means an effect on the human body, including an effect on one or more of the following:

(a) a biochemical process or outcome

(b) a physiological process or outcome

(c) a functional process or outcome

(d) growth and development

(e) physical performance

(f) mental performance

(g) a disease, disorder or condition.

It is apparent that many of these health effects are not nutritional effects and that the addition of a substance to achieve these health effects is not an addition for a nutrition purpose and consequently does not constitute "Use as a Nutritive Substance". This emphasises the importance of being very explicit about the purpose of adding a substance, such as Lactoferrin, to ensure that this is not inadvertently represented as a "nutritional purpose" when it is a "health effect" function (i.e., support the immune system) not related to essential nutrition.

When bovine Lactoferrin is added to dairy foods, it is added at levels (50-200mg of protein) supported by well-performed scientific studies to foods for infants and adults, to support outcomes related to immune system and other health effects, **and this is substantially below the level of protein which would be necessary to achieve a nutritive effect (protein)**:

i. Health effects in infant formula and foods for young children
   a. Lactoferrin and cognitive health [1]
   b. Lactoferrin and gastrointestinal immune system health [2,3]
   c. Lactoferrin and gut health effects in 12-36 months old [4]
   d. Lactoferrin and immune system health effects in infants and children - Meta analysis [5]

ii. Health effects in adults
   a. Lactoferrin and skin health effects [6]
   b. Lactoferrin and immune system health effects - Meta analysis [5]

Also, as noted above, the FSANZ website already includes details of 3 notified food health relationships, established by systematic literature review, between Lactoferrin and support for immune health. This provides further support for the interpretation that Lactoferrin is being used to achieve a health effect other than as a nutrient (protein).

Application A1253 does not identify a nutritional purpose for the addition of Lactoferrin. In fact, the application highlights the reason Lactoferrin is added to infant formula is to achieve health effects relating to immune support (and is therefore by definition, added for its health effect and not for its nutritional effects).

FSANZ's Call for Submissions following its assessment also recognises that Lactoferrin is added to infant products at levels that provide a health effect and not a nutritive effect. Indeed, the FSANZ assessment identifies one of these health effects as 'reduced severity and duration of infection', which is clearly a therapeutic effect, or alleviation of a disease, rather than a health effect. The FSANZ assessment report confirms that Lactoferrin is intended to be used to support a health effect, which would be consistent with the addition of bovine Lactoferrin as a normal milk component, and not as a substance used as a nutritional substance.

This supports the position that Lactoferrin is in fact a traditional food ingredient used to achieve a health effect benefit and is not a 'substance added to the food to achieve a nutritional purpose', and as such, should not be classified as a nutritive substance.

In conclusion, Noumi supports clarification in law as it relates to Lactoferrin quantities which can be

added safely to infant formula products. However, Noumi believes Lactoferrin should be categorised a 'traditional food' ingredient and not a 'nutritive substance' when added to infant formula, given its long history of safe consumption by babies from breast milk ingestion and via infant formula intake in other jurisdictions around the world and because the homology between human and bovine lactoferrin is high at ~70%. Importantly, Noumi's argument is that Lactoferrin is not added to either infant formula or other food products as a nutritive substance but is instead added to achieve a 'health effect', like immune health effects, gut health and/or skin health support, according to the clear definition of health effects outlined in Standard 1.1.2 of the Food Standards Code.

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Appendix 1 - Noumi's Lactoferrin production process flow detailed description

1. Skim Milk

Noumi sources its milk from the Goulburn Valley in Victoria, Australia. Raw whole milk is separated, and the skim milk is transferred to the Lactoferrin plant for processing. The skim milk is maintained at refrigerated temperatures throughout storage.

2. Clarifier

Noumi processes the skim milk through a Bacterial Removal Separator (Clarifier) that reduces the bacterial load in the raw skim milk.

3. Milk Filtration

The skim milk is processed through a series of filters that remove any remaining foreign matter, fat, fat-soluble compounds and insolubles. These filters become increasingly fine as the milk is processed through each, culminating in a 1 µm filter.

4. Radial Flow Column (RFC)

Extraction of the Lactoferrin from the skim milk is conducted through an ion exchange process where the skim milk is passed through radial flow columns containing specialised ion-exchange resin. The resin is composed of large, crosslinked agarose beads (100-300µm). The resin is tailor-made for industrial applications and the large particle size and physical stability of the base matrix allow the resin to be utilised in high volume commercial extraction processes. The ion-exchange capability of the resin binds the Lactoferrin from the skim milk for collection through the elution process.

The bound Lactoferrin is eluted from the resin using a series of increasingly concentrated sodium chloride buffer solutions, the highest of which has a concentration of approximately 10% w/v. The Lactoferrin eluate is collected and stored for further processing.

5. Ultrafiltration / Diafiltration Process

Lactoferrin ultrafiltration and diafiltration of the eluate removes sodium chloride ions from the Lactoferrin solution and increases the solids in the solution. Total solids and pH of the concentrate at the completion of this step is critical to maintain the native PUREnFERRIN® structure. Pasteurisation

7.

Pasteurisation is specifically designed to ensure food safety requirements are achieved in accordance with Australian regulations (Food Standards Australia and New Zealand). The pasteurisation step is considered a crucial step involved in maintaining the native stature of PUREnFERRIN® and is designed to minimise the heat profile of the Lactoferrin concentrate. To meet regulatory requirements, the concentrate must undergo heating to 72°C for a minimum of 15 seconds, or equivalent. Cooling of the Lactoferrin concentrate immediately post-pasteuriser is critical to the bioactivity levels of the PUREnFERRIN®.

6. Spray Drying

PUREnFERRIN® concentrate is processed through a multi-stage spray drying process that gently dries the Lactoferrin at lower temperatures than conventional spray drying processes. The first stage of the drying process is designed to remove most of the moisture from the concentrate forming the powder particle. This part of the drying process is specifically controlled using airflows, air temperatures and concentrate nozzle pressures to achieved specifically designed powder particles to meet customer needs and specifications. The second stage of drying consists of the drying fluidising bed where lower temperature air and air flowrates are used to gently condition the Lactoferrin powder, cooling the protein matrix whilst gently adjusting the moisture content to the desired level. The product is then passed through a vibrating sifter prior to packing.

7. Packing

The final stage of the process involves dispensing the Lactoferrin into specifically designed heavy foil pouches. The Lactoferrin powder passes through a metal detector and into the packaging material, which has excellent barrier properties, maintaining PUREnFERRIN® product integrity for the long sheLactoferrin life of the product. Packaging formats are typically 5 kg; however, this may vary depending on the customer.

Appendix 2 - Lactoferrin containing formulated supplementary foods for young children

NEURIO KIDS
Milk Powder with Lactoferrin

NEURIO KIDS
Milk Powder with Lactoferrin

SLAITE
Milk Powder with Lactoferrin

AUTILI
Lactoferrin Milk Powder

AUTILI
Lactoferrin Milk Powder

AUTILI
Lactoferrin Milk Powder

AUCOKO
Lactoferrin Milk Powder

Appendix 3 - Lactoferrin containing food for adults

WELL BOOST HOSPITAL
with Lactoferrin

PEAK Immune Powder
and Shake with Lactoferrin

PROFESSIONAL WHEY
LACTOFERRIN Powder