The Evolution of Personalised Nutrition: Regulation – Enabling and restrictive contexts and food safety

Personalised nutrition services are currently considered as “not regulated” anywhere in the world, and a number of studies have pointed this out repeatedly for over a decade. The scientific community that was driving PN science and the investigation of its merits and challenges has in the past 15 years proposed repeatedly conceptual frameworks and “guiding principles” that might be used as input for regulation of PN services (Adams et al., 2020; Grimaldi, 2019; Kohlmeier et al., 2016). However, these efforts have to date not been taken up by regulators, and explicit regulation of the sector needs still to be implemented. However, there are other regulatory areas that “surround” the PN space and may impact its evolution. In terms of regulatory remit definitions, it is important to distinguish between a wellness and/or lifestyle offering that would maintain or improve the existing health status of a PN customer, and services that are health offerings with the explicit aim to prevent or alleviate illness. This distinction is clearly made within EU regulation and has impacted PN service offerings in some countries.

In this section we present drivers and challenges of the wider regulatory context that surrounds PN. This also means, that the effect of other regulatory frameworks with indirect impact on PN may not have clear unidirectional outcomes with respect to the evolution of a currently unregulated area of activity in the sense of “drivers” or “challenges”. Hence these terms in the regulatory domain might be better called “enabling contexts” and “restrictive contexts”. It should be noted that our interpretation of “enabling” and “restrictive” can at this stage of UK regulation only be speculative.

As PN has evolved in its current form out of the medical domain some of its aspects are already covered by some existing regulation. The main aspects of PN services that involve some form of bio-specimen testing, and therefore can be considered a health offering, are the following:

1. Analytical validity of tests (technical accuracy and robustness etc)
2. Scientific validity of analysis that is used as basis for advice
3. Utility of the advice (will it enable a beneficial outcome beyond standard advice by dieticians and nutritionists)
4. Ethical, legal, social, and data protection issues

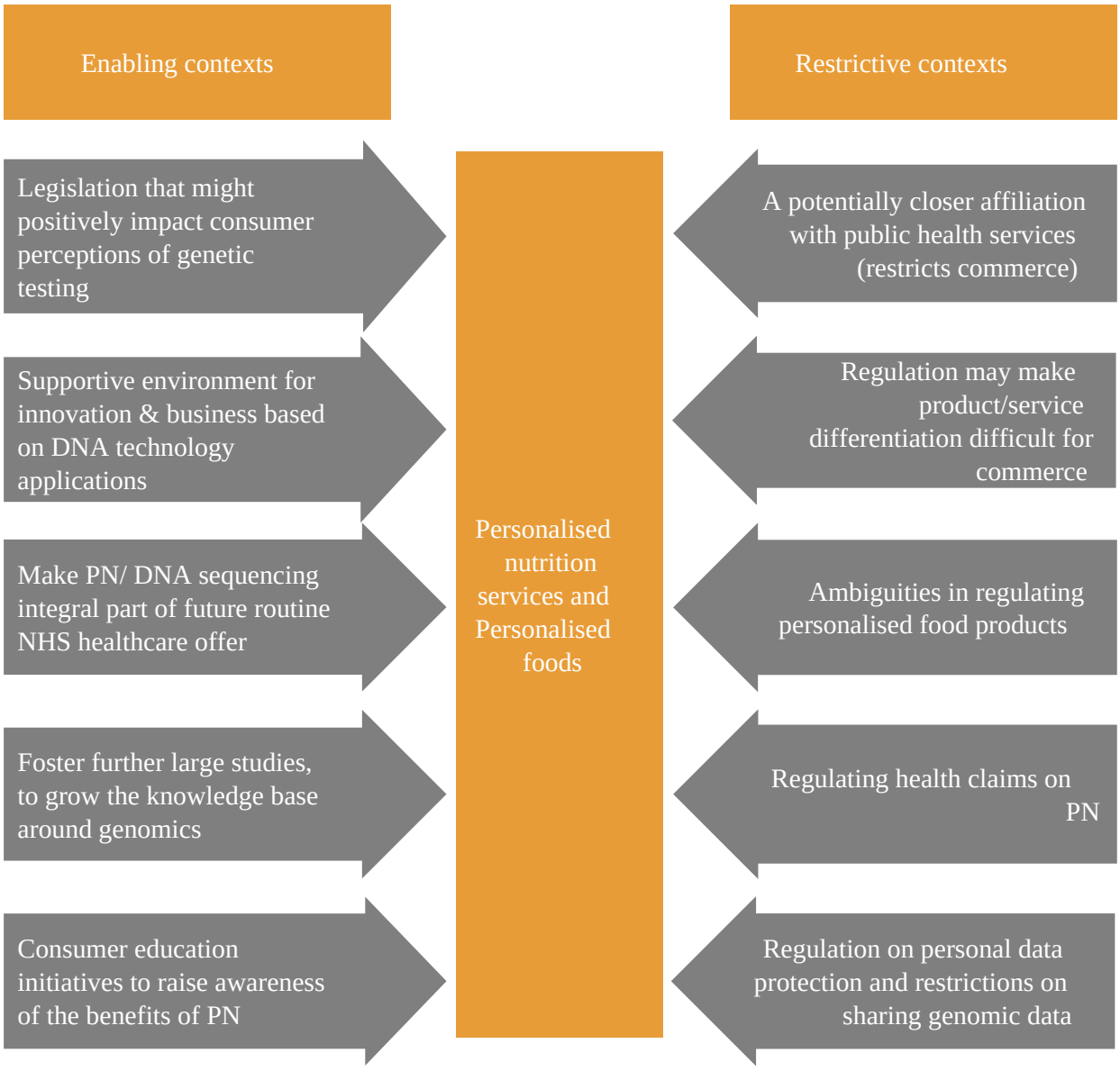
These domains are overlapping for example with existing UK regulatory frameworks that assess the validity of genetic testing in a clinical setting. The applicability and limitations of these regulatory domains for PN have been recognised for a while (Keith A. Grimaldi et al., 2017; Keith Anthony Grimaldi, 2019). In the UK, the following existing legislation would apply to most PN services, including those involving D2C testing (House of Commons Science and Technology Committee, 2021):

- the Consumer Protection Act 1987 and the Consumer Rights Act 2015 (which require products or services sold to consumers to be fit for purpose, as described, and meet certain minimum standards, covering aspects such as quality and safety)
- the UK General Data Protection Regulation (which covers the collection, storage, and use of data)

- the Human Tissue Act 2004 (which effectively bans DNA analysis without appropriate consent)
- the Advertising Codes (which ban adverts that are misleading, harmful, offensive, or irresponsible, and are enforceable under the Consumer Protection from Unfair Trading Regulations 2008 and the Business Protection from Misleading Marketing Regulations 2008)
- for commercial genomic tests with a medical purpose: the Medical Devices Regulations 2002 (which set out essential requirements for in-vitro diagnostic devices placed on the market, such as requirements on safety for users and for performance to match the manufacturers' claims).

It is currently not clear to what extent players in the UK PN market are aware of or are explicitly following existing legislation. Studies investigating current standards in the UK have to our knowledge not been undertaken.

Figure 16 Enabling and restrictive regulatory contexts for PN



Enabling regulatory contexts

Legislation that might positively impact the consumer perception of genetic testing

The UK is a world leader in DNA science and technology and Government has recently passed the strategy report “Genome UK The future of healthcare” with the aim to create a supportive environment for innovation based on DNA technologies, applications, and DNA technology businesses in the UK, and to make DNA sequencing an integral part of future routine healthcare offerings of the NHS. In addition the framework should foster further large studies, such as sequencing all 500,000 individual samples of the UK biobank, to grow the knowledge base around genomics for the benefit of human health (HM Government, 2020). The importance of public trust in genomics was recognised and expressed by the pledge to: “establish a gold standard UK model for how to apply strong and consistent ethical and regulatory standards”. A major goal of the proposal was to implement personalisation of medicine across the NHS. In parallel, large public engagement and information initiatives are promised to educate the public about the benefits of genomics applications. Implementation steps were published in the following year (UK Government, 2021). The role of commercial players in the genomics space was only mentioned in passing by expressing the intention to enable industry growth through start-up support. Overall, it is expected that these efforts might lead to increased public awareness of personalisation approaches based on genetic analysis, and hence might have a positive effect on commercial PN providers.

Specific concerns related to commercial D2C genomic testing have been raised by a House of Commons Science and Technology Committee report published in 2021 (House of Commons Science and Technology Committee, 2021). This is important, because D2C testing involves medical devices that are used for collecting, extracting, and sequencing DNA. As Government has after the Brexit transition period decided to not implement new EU regulation due to be implemented in 2022, currently the UK legal framework for commercial D2C testing is unchanged and based on earlier legislation as outlined above, with the Medicines and Healthcare products Regulatory Agency (MHRA) considered the responsible regulator for devices used in the PN sector. In this context, the report by the UK House of Commons Science and Technology Committee identified a number of problematic areas that needed addressing in order to progress beyond the currently ill-defined legal situation, and the following recommendations were made:

- D2C tests should be required to be subject to greater pre-market assessment by an external body to assess clinical and analytical performance of the tests. Currently most providers can self-declare whether they believe their product meets standards within current legislation.
- Technical standards for D2C tests should be defined in collaboration with Genomics England and the NHS. Ideally, test providers should then voluntarily meet such standards in order to reduce false positive/false negative rates, and gain trust by consumers.
- Obligatory information about different kinds of consequences of test results, not necessarily linked to the specific service offering, should be provided, as well as support in cases of “unwanted” or distressing results. This includes for example potential consequences for family members, or the need for some results to be assessed under medical supervision.
- The UK’s current data protection framework needs to be re-assessed whether it is fit for dealing with a growing market of confidential health related consumer data, including looking into risks and opportunities presented by novel technological developments.
- It should be considered whether there should be restrictions on the use of D2C tests for testing asymptomatic children or for prenatal testing.
- The scope of regulation needs to be re-assessed in particular for companies that sell products in the UK, but conduct testing and analysis outside of the UK, and companies offering analysis of genomics data obtained from third parties.

These recommendations correspond very well with what has been recommended in the academic literature for over a decade. Should Government decide to act upon these recommendations then this might lead to a more trustworthy commercial environment for genetic testing with better quality products for consumers. In addition, a clear regulatory environment might encourage further commercial activity in this sector. However, given the usual time frames in politics and legislation, this may be at least five to ten years away.

Restrictive regulatory contexts

Potentially closer affiliation with public health services

A potentially closer affiliation with public health services in the UK could emerge from above outlined regulatory intentions, which might create a regulatory environment that could make it more cumbersome for PN businesses to enter the market. Moreover, as all potential providers will need to adhere to the same science base it will be difficult to differentiate from other providers and create a distinct offering. Developments in EU countries might be instructive for possible future outcomes in the UK. The current EU frameworks impacting PN are fragmented and no EU-wide piece of legislation to regulate PN exists. Genetic testing and medical devices for genetic and other bio-specimen testing are regulated in the EU by the Medical Device Regulation, and the In vitro Diagnostic Medical Device Regulation (IVDD/IVDDR), with the latter differentiating between testing for medical purposes (health offerings) and testing outside of traditional healthcare settings for the purpose of providing information on disease disposition. While the device aspect of PN is covered by this legislation throughout the EU the ways genetic testing can be offered and by whom is not, as issues of “medical supervision” and “informed consent” are subject to national legislation and hardly harmonised across the EU. Direct-to-consumer testing is regulated quite differently across the EU and has to do with public sentiment around genetics and trust in science in general as well as with different cultural norms around medicine and health. For example, France and Germany have restricted all genetic testing for health purposes to “medically supervised use”, which in effect prohibits D2C testing in a commercial setting (Röttger-Wirtz & De Boer, 2021).

Ambiguities in regulating personalised food products

Ambiguities in regulating personalised food products that are associated with health claims might lead to a persistent regulatory vacuum that might have a negative impact on consumer trust in PN products as well as on businesses due to regulatory uncertainty. Currently, PN providers either do not offer personalised food at all, or do so by selling personalised vitamin formulations and supplements. Although supplements do not need to be licensed or registered in the UK, they need to comply with the General Food Law and are subject to the provisions of the Food Safety Act (FSA remit) as well as the Food Information Regulation 2014 and the Food Supplements (England) Regulation 2003. Companies selling supplements need to register as a Food Business Operator (FBO). In the context of PN it is important to point out that within UK law, supplements are defined as ‘any food the purpose of which is to supplement the normal diet and which is a concentrated source of a vitamin or mineral or other substance with a nutritional or physiological effect, alone or in combination and is sold in dose form' and ‘they are not medicinal products and as such cannot exert a pharmacological, immunological or metabolic action. Therefore, their use is not intended to treat or prevent diseases in humans or to modify physiological functions’ (our emphasis). This latter definition makes explicit that supplements are not supposed to be sold with the intention to act on the body in similar ways like a medicine. Most PN providers however make claims regarding disease prevention, or effects on immune and metabolic function, placing these at the core of the PN offering. This discrepancy would need to be addressed by regulators such as the FSA in order to provide clearer guidance for the PN sector on how to stay within legal boundaries when making claims.

Existing EU legislation can give a good illustration of the issues involved and might be seen as instructive for the UK context. The main ambiguity arises from the blurred boundary between food and medicine in the case of a personalised food offering with claimed health benefits. The EU General Food Law (GFL) defines as food: “any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans”. This has to be contrasted with nutrition that is associated with claims that make its effect on health so prominent that it would fulfil the definition of a medicinal product. According to article 1(2) of Directive 2001/83/EC medicinal products are defined as: “any substance or combination of substances that either is presented as having properties for treating or preventing disease in human beings, or that may be used in or administered to human beings, either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis” (Röttger-Wirtz & De Boer, 2021) (our emphasis).

Thus, the classification as medicinal product either follows from the presentation of the product or from its function. In cases where it is unclear whether a product might be qualified as a medicinal product or as another regulated product (e.g., a food product), then the application of the pharmaceutical legislation takes precedence in EU law. This hierarchy of regulatory frameworks within the EU is also confirmed in the GFL, which in Article 2(d) excludes the application of the GFL to medicinal products (Röttger-Wirtz & De Boer, 2021). Should the UK wish to regulate personalised food products then very different regulatory frameworks need to be considered in the cases of medicine or food, but more importantly a clear stance needs to be taken on how to make this distinction for PN products in the context of UK law.

Existing UK food safety regulation and standards defined by FSA would apply to PN products that can be classified as foods, such as supplements. However, this regulatory framework is usually applied to food items that are sold to larger populations, and not to foods in effect sold to one person. Hence food safety issues for the wider public should not arise, as in theory only the person for whom it was personalised should eat it with the expectation that it will positively impact that person’s health. Potentially other people with very similar personalisation parameters might eat the same formulation of food item with similar benefits. In contrast, there could be situations in which a personalised food item consumed by a person for whom it was not tailored for might suffer immediate or short-term negative health effects. It is understood that any food product, personalised or not, coming to the UK market needs to comply with regulatory standards for any food product first. What is not clear however is to what extent PN providers would classify their products in the current regulatory situation as foods or as supplements. This situation might cause confusion not only among potential customers, but also among providers, who will probably tend to choose the easier regulatory framework to follow, or will avoid offering food products altogether because of these ambiguities.

Regulating health claims on PN

Regulating health claims on PN may be attempted by future UK legislation and would affect the way PN services are offered and how providers can operate. In the UK, as in the EU, consumers should be protected from false and unsubstantiated claims about a product. As with other products the legal requirement that advertisement, labelling, presentation including packaging and given information shall not be misleading applies certainly to PN offerings. This can be considered particularly important in this sector because consumers cannot be expected to have the required scientific expertise to make a truly informed choice. Clarification on permitted claims for the PN sector would be helpful to build trust with consumers and enable confident decision making for businesses.

In the UK, health claims related to nutrition are regulated by the Nutrition and Health Claims (England) Regulations 2007 and Regulation (EC) 1924/2006, updated following Brexit on 1 January 2021 with ‘The Nutrition (Amendment etc.) (EU Exit) Regulations 2019’ and ‘The

Nutrition (Amendment etc.) (EU Exit) Regulations 2020'. After Brexit the responsibilities for the risk assessment and risk management processes covered by nutrition legislation were transferred to bodies in Great Britain. As regulatory oversight over nutrition legislation is a devolved responsibility in the UK, the Department of Health and Social Care is responsible in England, the Welsh Government in Wales, Foods Standards Scotland in Scotland, and the FSA in Northern Ireland. This regulatory framework also covers claims to reduction of disease risk and claims based on newly developed scientific evidence. Although UK Government stated in above post-Brexit amendments to be committed to upholding EU and international standards, it might be useful to look at what EU legislation already covers in the PN space as this might inform future regulatory decision-making in the UK.

The EU Food Information to Consumers (FIC) Regulation would cover any food product sold by a PN provider and not only prohibits any misleading information about contents and quantity, but also explicitly prohibits "attributing to food any effects and properties it does not possess" and "to attribute to any food the property of preventing, treating or curing a human disease, nor refer to such properties". This distinction again reinforces the boundary between food and medicine and will basically prevent marketing of food products personalised via genetic testing as "reducing disease risk".

The second piece of EU legislation relevant to health claims is the Nutrition and Health Claims Regulation issued in 2000 with the rise of "functional foods" and food supplements. The regulation distinguishes between nutrition claims (such as ingredients, calorific value etc) and health claims that link a food or food ingredient to health. Health claims on the health promoting activity of certain foods or ingredients need to be "authorised health claims" that are specified by the legislation and their health effects need to have been proven by prior generally accepted scientific evidence. As "promotion of health" is an integral aspect of PN it matters which kind of claims can be legally made, as this affects the core value proposition of the PN offering. The legislation specifies three categories of health claims, namely functional claims, disease risk reduction claims and children's development claims. Under functional claims fall claims that refer to: a) development, growth, and functions of the human body; b) psychological and behavioural functions of the human body; c) reducing or controlling body weight or suppressing/reducing hunger as well as reducing calorie intake. Again, these claims can only be legally made when they are listed authorised claims backed up by scientific evidence.

Disease risk reduction claims for personalised food items need to be carefully crafted within these regulatory boundaries so as not to transgress the food/medicine boundary. For example if claims are made that the disease risk reduction would be an immediate effect of consuming the personalised food (after disease risk was first established by a genetic test), then the food would be seen as being presented as a medicine. In this context the disease risk reduction claim needs to specifically state whether the disease risk is multi-factorial, and if so whether influencing one factor with a given personalised food or ingredient will change the overall risk. In addition, it is forbidden: to imply that not eating the personalised foods in question will negatively impact health; to state specific amounts of "expected" or "predicted" weight loss; to make claims based on statements of individual doctors or other health professionals, such as dieticians. Other requirements for making legal health claims include additional statements that must be made together with the main claim. This includes the reference on the importance of a varied and balanced diet, how often and how much of the food item in question needs to be consumed to achieve the claimed health effect, as well as any safety warnings who should not consume the food, for example in relation to allergies, or small children etc. Any claim that certain personalised food items would be "generally healthy", or "health promoting" in a general sense can only be made when this claim in relation to that food is on the list of authorised health claims.

In particular, in a PN context disease risk reduction claims are usually made via complex analysis of many phenotypic variables specific to the consumer, and hence are based on a multi-factorial analysis. As currently health/disease risk reduction claims can only be made one ingredient or

nutrient at a time by specifically showing scientific evidence for one causal nutrient-health interaction, it is problematic how health or disease risk reduction claims can be formulated in simple claim statements for consumers. So far no listed authorised claim has been submitted that would make it a legal statement that a certain nutrient can affect the genetic predisposition for certain diseases. Again, for most PN providers that is seen as a fundamental aspect of their offering.

One way to market PN products could be via catering to micro-markets of consumers who share certain phenotypic characteristics as defined by PN data analysis. This would mean that a claim would be applied only to a specific sub-population, as is currently regulated for example when making claims specific to children, pregnant women, the elderly etc. In such an approach the claim needs to be based on scientific evidence specific for that sub-population and given that the difference between such sub-populations and the general population can only be defined in terms of subtle genetic and other phenotypic differences, it is currently questionable whether these would be considered by legislators as sufficient to warrant definition of novel sub-populations. EU regulation related to such an approach would be Regulation 609/2013 that specifically deals with targeting of food products to specific groups with special dietary needs, such as foods for infants and children, for specific medial purposes (for example in an intensive care setting), or intended for weight loss in cases where it can replace a normal varied diet. This regulation applies mostly to clinical settings or the care home sector when people cannot consume normal food due to their medical conditions and the specified foods are usually consumed under medical supervision. It is therefore unlikely that regulators will consider defining sub-groups of healthy people sharing similar characteristics as defined by a PN provider. Moreover, professional athletes and diabetics have so far been explicitly excluded from this regulation for sub-populations with special dietary needs (Röttger-Wirtz & De Boer, 2021).

This overview of regulatory issues was intended to demonstrate the areas of regulatory intervention that would need a clear resolution with regards to existing UK and EU legislation, should UK legislators want to decide to support commercial PN efforts in the longer term. Given the above complexities, any intention to impact the evolution of the commercial PN market needs to be taken up immediately as it may take considerable time to find simple actionable regulatory solutions. In the meantime, the current regulatory situation might lead on the one hand to a proliferation of over-promising providers making possibly even unintentionally, illegal claims about their offerings, while consumer trust and interest in such offerings may erode, and new businesses in the sector will not be able to grow because of regulatory uncertainties.

Personalised nutrition and food safety

Given its current state of evolution PN may pose food safety risks in two areas, one still hypothetical und unexplored, and the other related to better understood issues to do with the longer-term consumption of supplements. As PN is currently to a large extent nutritional advice it may appear that there are no safety risks involved beyond the risks of following advice given by nutritionists or dieticians. It is assumed that such advice is based on scientific evidence from large population studies, so it is always likely to have some margin of error when applied to individuals.

However, what is hard to assess at present is whether longer-term negative health impacts may arise from adhering to advice that is generated by complex PN analysis and supposed to be more suitable for a specific individual, in cases when the advice given by PN providers is in fact based on unintentionally faulty scientific analysis. This situation is not unlikely given the complexities around the scientific foundations and data integration of PN as discussed in chapter 4. As consumers will have generally limited knowledge around the science, and few possibilities to evaluate the information they pay for, it will be important to define what might constitute fraud in this area. These considerations are currently not within FSA remit, but the FSA might wish to consider whether it would be worthwhile, in collaboration with other regulators such as the

Department of Health and Social Care, to establish certain standards at the advice level for an emerging industry that is associated with food.

In cases where providers sell supplements and vitamins in addition to personalised advice certain well understood risks for consumers may exist. These can arise from low quality of source materials, inappropriate storage or packaging, contamination during production, erroneous or fraudulent labelling etc. all of which are within FSA remit and are covered by existing legislation.