NeoNatural Flavors: Social Factors Affecting the Adoption of Microbially Derived Flavorants

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Introduction

The food supply of western nations has drastically changed in the past 150 years, as the principles of industrial production and processing have become the only means of achieving both the scale and variety demanded by consumers (Arizpe et al., 2011). One of the key links in this supply system is the use of additives to achieve preservation, flavoring, and presentation goals. The central body in the United States which regulates these spaces is the Food and Drug Administration. This government agency was started in the progressive as a mouthpiece for the public to enforce cleanliness regulations upon food manufacturers (Eaglstein, 2014). Since then its scope has increased massively, with medicines, medical devices, seafood, exotic meats, tobacco, and food additives all being under its jurisdiction (FDA, 2023). Within the food side of the FDA, roles include inspection of food processing conditions, consumer information regulations, and regulations of accepted and banned foods and components. As part of its domain of consumer information, manufacturers are required to list the ingredients within a processed food, with the exception of flavorants. Flavorants are grouped together as either natural or artificial, depending on their means of production. Traditionally, natural flavors were created using solvent extractions and pressings to plant or meat products, while artificial flavors are created from petroleum derivatives and organic synthesis (Sluss, 2009). An important compositional difference between these two processes is the scope and complexity of the liquors produced. Natural flavors contain a variety of chemicals in small concentrations while artificial flavorings take the primary elements within these natural blends and amplify their concentration to maintain the main flavor notes of the source blend. Ignoring the safety risks presented with the introduction of novel compounds from artificial flavorants, this was a useful system because the categorization between these two was clearly defined and consumers had a clear understanding of the differences between the two.

Technological advancements within the biopharma sector have eroded these differences, and regulation efforts have not adjusted to these realities. The use of separation techniques for fermentation broths, and the ability for genetically modified organisms to produce specific compounds in higher concentrations has rendered a new flavorant type to become economically viable and widespread (Braz, 2010). This new flavorant type presents aspects of both previous types, with the biological origin of natural flavors and the low variety high concentration chemical blend of artificial flavors. The net result is the same mixtures found in artificial flavors, but moved into the biological space. These differences create a product which deserves a unique classification. How did this technology go from discovery to mass adoption without any major safety validation for its outputs and any significant alterations to the regulatory environment?

A major reason for the usage of cultured flavors is their interactions with legal codes. Under current FDA regulations, the processing technique is the only factor of classification, and due to their biological origin, these microbially generated flavorants are classified as natural flavors (CFR, 2023). The public was trusting and supportive of the change from artificial to cultured flavors, as the term natural carries strong psychological significance. Because neither the public nor the government devoted significant resources to shaping the implementation of biopharma processes in the industrial production of flavorants, manufacturers were free to completely choose the nature of their usage, and over time the boundaries of usage ossified into its current form.

Background and significance

A central concept within the American psyche is the consumer assumption of risk (Griffin, 2023). This assumes that an appropriately informed consumer is liable for their own decisions and can be trusted to act within their best interests. Central to this concept is that the consumer must be informed to make these decisions. Examples of this include warnings on cigarettes and alcohol so consumers can gauge if the negative health effects are justifiable for the experience they are purchasing. These warning systems are most useful at preventing a few, high level dangers for either the general populace or specific groups. If the threats produce chronic effects, and require a high level of knowledge and effort to understand their effects if they were even investigated in the first place, the notion of the informed consumer assuming risk is utterly destroyed. This breach of the informed consumer is even more glaring when considering intersectional concerns.

Class is a major predictor when considering processed food consumption (Pechey et al., 2016). Processed foods are cheaper, longer lasting, and require less time to convert into meals; all of which are desirable attributes for individuals who have scarce money, time and energy. Hand in hand with the consumption of these processed foods is the consumption of their additives, including flavor additives. Another group which disproportionately consumes processed foods is children (Vandevijvere, 2018). Children are frequently conditioned to enjoy the stronger and sweeter flavors frequently presented by processed foods and select it compared to other options. This represents a greater risk of chronic effects due to additive usage as the lower weight of children results in a higher adjusted dosage, and children are more vulnerable to hormonal issues and pollutants while growing (Vogt et al,. 2012). These combined factors can result in health issues for low income children, which leads to suffering and could perpetuate income inequalities.

Underprivileged groups also frequently are focused on fixing short term issues so they do not have the ability to consider chronic or insidious threats (Ablev, 2009). This places the burden of accurately predicting and communicating the threats caused by certain chemicals to government regulatory experts. The FDA has failed in this mission in both counts. In a cost saving measure under the Generally Recognized as Safe (GRAS) guidelines, companies are allowed to submit their own toxicological studies with their application for a GRAS additive (Zwanenburg et al., 2014). This represents a huge conflict of interest for the flavorant manufacturer, and cannot be trusted as legitimate scientific data. Once this additive clears the guidelines, it joins a long list of chemicals which can be added provided that they are labeled in the ingredients or considered a flavorant. Once it clears or if the foodstuff is described as a dietary supplement, GRAS ingredients are placed in weight percentage order like all other ingredients, with consumers unable to assess the risks associated with each component. The many loopholes within the ingredient system render it nearly worthless aside from determining allergy information. The end result is an environment where manufacturers have leverage to only reveal the information at their discretion, and novel chemicals can enter the public's food supply through the use of flavorants.

Once flavorants are introduced into the food supply, the odds of their effects being determined in a reasonable timeframe are slim to none. Additives nearly always arrive as blends, and teasing out individual chemical exposure effects is nearly impossible due to the varied nature of many diets (Brown et al,. 1998). Furthermore, the chronic nature of dosage means that symptoms might not appear until years of regular consumption of a particular additive. As an example, trans fats persisted in the food stream for more than 70 years before the heart issues

associated with their consumption led to regulatory change (Amico et al,. 2021). This threshold for investigation into an ingredient already cleared would only really occur after a significant death toll was achieved. This places a higher importance on being a proper gatekeeper for these ingredients lest they disrupt the health of an entire generation.

Methodology

Societally sprawling topics such as the ability of a regulatory body to adapt to changing technologies can quickly become overly focused and miss the broader message. To prevent this outcome from occurring, sociological frameworks can be used to focus the problem to aid at arriving at an understanding. The social framework most relevant in this instance is social construction of technology. Social construction of technology posits that the implementation of a new technology is determined by a series of compromises between the major stakeholders of its usage. After this initial compromise is taken, the technology builds up an inertia, and it is more difficult to change the use cases, especially in removing current use cases (Bijiker, 2012). Central to this theory is understanding the factors which may make the voices of important stakeholders less resonant. This is a major factor at play for the introduction of cultured flavorants. New technologies can present themselves as black boxes where the individuals debating their usage do not fully understand the nature of the subject. Chemical additives to food can be divisive for that very reason, as the nomenclature and physical effects of additives presents a high information barrier leading a consumer confused and looking for guidance. The typical guidance for regulatory efforts is effectively leaving it to the experts and letting the wheels of technocracy iron out the kinks. This is an effective strategy in many cases where the learning curve is steep and the regulations are thorough. A danger within this logic is the supposition that the regulations are thorough. This attitude can lead to inaction and remove a vital check on manufacturing power. A lack of clear direction can also be a hindrance to vote with your dollar style campaigns. Nearly all processed products contain multiple additives and flavorants, and choosing an unrefined ingredient based diet is beyond the ability of most individuals due to time and resource constraints.

The second check on manufacturing power during the implementation of culture based flavorants is regulations through the FDA. The FDA has the purview to create and enforce regulations on additives. Both of these tasks represent expenditures of resources for thankless tasks which voters and administrations are unfocused upon. Regulatory authorities are about effectively managing risk. Risk management is based on reducing the frequency of disasters to manageable levels while also letting businesses run with as few regulations as possible. A major deciding factor in the moral calculus of what acceptable risk entails is optics management. A public disaster is much worse for an agency than a private one, which could serve as an incentive to avoid investigation of systems which appear to be working (Seeger et al., 2019). This can be compounded if the testing to verify the components of the system is an expensive use of resources in a climate of cutting budgets and deregulation. The inertia and avoidance on behalf of the FDA has resulted in unchecked power of manufacturing authorities due to large loopholes within the current system deliberately placed to encourage innovation.

In addition to framing the problem, social construction of technology also presents a means of adjusting the process to arrive at a less unbalanced solution. The compromise and conversations between the major stakeholders can be achieved if a critical mass of voters force the issue of flavorant regulation. Ideally this occurs before a disaster is needed to galvanize the public. SCOT also presents a means of determining the causes of reluctance of oversight in both

consumer and government entities and the eagerness of implementation of manufacturing entities. The information supporting this analysis will be provided through a combination of policy review and academic sources. Motivations of voter groups are best understood through the psychology of risk analysis, cultural factors and survey responses. The government speaks through the text of their laws and the funding of their departments. These allocations of resources can be reasoned backwards to determine motivations. Lastly, insights about the pace of development within the food industry due to intellectual property protections, a high degree of supplementary goods and basic rules of economics can be used to understand the pressures of manufacturing.

Literature Review

While the FDA is a truly massive agency, the scope of activities that it must oversee can leave blind spots. Over half of the funding of the Agency is directed towards the drugs and medical devices avenue, and the upper leadership has historically been dominated by members of the drug side (DHHS, 2022). It has been reported that a common joke among members of the FDA is that the true name of the agency is the "Federal Drug Administration" (Oliver, 2023). Within the food side, FDA efforts are largely spent on public health campaigns and process monitoring. To give an example of how additive testing ranks, a division was created in 2021 to "Investigate Emerging Chemical and Toxicology Issues". The primary goal of this task force was to investigate the effects and detection methods of polyfluoroalkyl substances (Pfas), a well known hormone disruptor used in nonstick coatings for 50 years (Woodcock, 2021). The funding for this task force is less than the amount allocated to investigate cannabis usage effects, and equal to the amount given to a means of determining shrimp quality through machine learning. The toxicological equivalent to this task force on the drug side had 14x the yearly allocated resources in 2023.

Customer preferences are a vital component of effective advertising campaigns, so much research has been conducted into determining how risk is properly conceptualized. This risk is confounded by several factors inherent to the food industry itself, as investigated by Knox. Of particular importance is a strong familiarity bias, with foods eaten without acute illness being deemed safe (Knox, 2000). This willingness to ignore both chronic effects and repeat risks gives a huge benefit of the doubt when eating a food previously eaten. This food memory also applies to variations of the same food. As a result, reformulations of a processed product can pass through a consumer's risk assessment process without significant notice. Other risk biases also play major roles in adopting new foods. Americans in particular are noted to have increased optimism of their own personal outcome, and are less likely to trust an authority figure when they are presented with information about their food being unsafe. Another strong factor affecting consumer confidence in a foodstuff is the naturalism bias. An investigation into the roots of naturalism in food by Li determined that the perceived "naturalness" of a food is more dependent on a food's processing history than its actual composition (Li et al,. 2012). Additional survey testing showed that individuals will choose the naturally occurring option between two identical products for both single ingredient products and pollutants. Companies are more than willing to cater to these desires, and popular foods such as cheetos, macaroni and cheese, and energy drinks have made explicit advertising statements when artificial flavors are replaced with natural flavors.

Food manufacturers have strong financial incentives to be opaque to competing businesses, and are accidentally opaque to consumers. IP law is notoriously weak for both

restaurants and food manufacturers, due to competition between these sectors being perceived as encouraging creativity (Haider, 2021). This encourages most manufacturers to file their formulas as trade secrets rather than protected entities. This would be safe if the ability to reverse engineer said product were difficult. Food processing techniques are relatively restricted, and the main ingredients of a product are written on the packaging. This leaves flavorings as the sole bastion preventing identical knockoffs.

Another activity of food manufacturers which has resulted in a large degree of study is the means in which they affect policy and restrict regulation strengthening. The first significant attempt to regulate the space occurred in the 1958 Food Additives Amendment to the US food drug and cosmetics act (Zwanenburg et al., 2014). This act originally planned to force all food additives to have animal testing before their use could resume usage. Food manufacturers successfully fought this back resulting in the generally recognized as safe exemption. The GRAS exemption operated on the logic that many ingredients were used infrequently, had significant timeframes of their usage and were in small quantities; therefore, were most likely fine enough for public consumption. This grandfather clause has since been expanded to include novel compounds. As the list has grown, the inertia to testing these compounds becomes larger, and the FDA becomes more reluctant to spend money on conducting this testing.

Discussion

While the FDA has oversight for premarket screening of additive compounds, its efforts have not shown a significant enthusiasm for the task. The wide scope of the agency forces funding to be stretched in many directions, and a leadership disproportionately composed of drug side members ensures that food additive testing is not taken as a high priority. For example the toxicology division on the food side is a relative newcomer to the agency, only receiving an explicit independent funding in 2021. The drug toxicology division in comparison receives 14x the funding and therefore can conduct many more investigations before products are brought to market. In order to stretch its dollars and work hours as far as possible, most additive decisions are made with either industry funded studies, or no studies at all. Compounding this problem is the list of chemicals which have been introduced during this period creates a backlog if testing were to occur. The required facilities to both keep up with the current series of additive applications and begin to decrease this list of chemicals of unknown toxicity represents a significant inertia to fixing this issue. Without the funding or capabilities to test new additives, and a precedent of passing applications through without these trials, the FDA has no leverage to push back on questionable acceptances.

The priorities of the government and its regulatory agencies are indirectly caused by the will of the public. As a result the actions of the government reflect the fears and desires of the populace as an average. The low priority of the FDA to regulate additive space is due to an inability for the public to process these additives on a threat, agree on a desired outcome, and mobilize political capital to make it a priority. On the first front, most Americans have eaten highly processed foods for their entire lives at this point and will not view the processed food as a significant health risk. If they do view it as a risk, the words natural flavors will put them at ease and they will blame a different ingredient as the source of their ills. Even if the risks of cultured flavorant usage were determined as a priority, obtaining a consistent policy goal would be difficult. Many consumers would be displeased with government attempts to assert more control over their food choices, and the space is still too technically complex to have a specific boogeyman chemical to rally against. Entrenched chronic problems with unclear primary effects

are notoriously difficult to unify democracies towards solving. Any solution would be slow, expensive, and could take away the option of choosing an individual's favorite food. A system that doesn't have quick results, costs money, and can lead to a personal inconvenience will be difficult to vote into law. The issue of this avenue being controlled by an executive regulatory agency adds an additional layer of complexity and separation from the public that would slow any alterations even further. Direct economic action is also infeasible here, as the current regulatory environment does not allow for consumers to tell where cultured flavors are even used.

In contrast to both the FDA and voting public being indifferent to cultured flavor usage and introduction, food manufacturers require it for their very survival. Processed food is built off of brands, and if brands are unable to make flavor profiles that distinguish themselves from the competition or emulate an experience at a lower cost, the risk of large inventory losses is high. The number of source ingredients that provide the bulk of a food is much lower than the flavor options that can be created. As a result, the only way a brand can make a significant impression is through flavorants. Because this is such a vital part of the business, manufacturers have no option but to embark on a technological arms race with their peers to produce the most popular flavors at the lowest cost. As a voice enthusiastically embracing biopharma technology in the production of flavorants, and with no significant opposition to cultured flavorants being present, manufacturers co-opted this technology to their own means. This resulted in artificial flavors being rebranded as natural flavors, and new products being created with enzymatic methods. These products and these flavors have now been enjoyed by millions, and the usage of these processes within the manufacturing space are commonplace enough that the window of technological alteration has narrowed. As an artifact of this, flavorants of unknown health effects are consumed on a large scale, and customers have no means of determining what or how much of it they are having.

Conclusion

Culture derived flavorants are a new technology which reached mass adoption without any significant regulatory or safety verification barriers. This is a useful technology in the eyes of manufacturers, as it allows them to produce high purity specialty chemicals through microbial means rather than organic synthesis. This gives them a competitive edge by reducing some production costs and improving the optics of their product. Due to the additive regulations being low on the list of FDA priorities, the FDA has taken a very passive approach in both screening and labeling of flavor additives. The wording of natural flavors has resulted in a decreased perceived risk in consumers, as the nuances of extracted versus cultured flavorants is not explained. The health risks of these cultured flavors remains unknown, as cultured flavors contain the same higher doses of a few chemicals that artificial flavors do, and neither has had significant and unbiased testing of the individual components of their flavor blends.

The benefits of using cultured flavors by manufacturers compared to a lack of urgency in both the public and government has resulted in a hidden widespread adoption of these technologies. The inertia of this adoption means that cultured flavors will remain an aspect of flavoring processed foods and cannot be removed. The key to having a more honest integration of these technologies into the food system depends on how the public can be properly informed to be able to assume the risk of eating the products generated through these methods. This can be accomplished through two main methods. The first of these methods is to create a third flavoring category separate from both natural and artificial. This cultured flavor category will maintain the

secrecy needed by manufacturers while also decreasing the naturalism bias present in the current regulations. The second method to improve consumer assumption of risk is to create a procedure to test the chemicals within the generally recognized as safe list and gradually sort them into usable and unusable compounds or simply classify them by risk. If these goals can be achieved, consumers can properly assume the risk of individual processed foods and latent health effects of additive usage could be reduced. Lowering these health risks would improve our industrial food supply and the health of the most vulnerable within society.

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