DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food Labeling; Gluten-Free Labeling of Foods

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Final Regulatory Impact Analysis

Regulatory Flexibility Analysis

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Final Regulatory Impact Analysis

A. Introduction

The Food and Drug Administration (FDA or we) has examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Orders 12866 and 13563 direct agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). We believe that this final rule is a significant regulatory action under Executive Order 12866.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Additional costs per entity of this final rule are small but not negligible, so we conclude that the final rule could have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $139 million, using the most current (2011) Implicit Price Deflator for the Gross Domestic Product. We do not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

On January 23, 2007, we published a proposed rule to define the term ‘‘gluten-free’’ for voluntary use in the labeling of foods. In the 2007 proposed rule, we analyzed the economic impact of the proposed rule and several other options for the definition of “gluten-free” (72 FR 2795 at 2804). This economic impact analysis explains and further revises the analysis set forth in the 2007 proposed rule.

B. Need for Regulation

This regulation is mandated by statute, and it is a response to information asymmetries and market failures that result in consumers being at risk for harm from products that contain high levels of gluten but are labeled as being "gluten-free."

Section 206 of the Food Allergen Labeling and Consumer Protection Act of 2004 directs the Secretary of the Department of Health and Human Services to issue, in consultation with appropriate experts and stakeholders, a rule to define and permit use of the term ''gluten-free'' on the labeling of foods (Ref. 1).

Gluten is a protein found in wheat, barley, rye, and their crossbred hybrids (Ref. 2). Wheat gluten is generally recognized as safe (Ref. 3), and gluten-containing grains are staples in the food supply (Ref. 4). Because of this, many foods contain gluten-containing grains or ingredients derived from them. Additionally, many foods contain gluten even though they do not contain any gluten-containing ingredients, because of cross-contact with these ingredients (Ref. 4).

People with celiac disease may be harmed by consuming gluten. One way for them to avoid harm is to consume a gluten-free diet (Ref. 2). Many foods bear a "gluten-free" (GF) labeling claim to advertise that their food is appropriate for individuals with celiac disease.

Private markets operating within the framework of the legal system promote the health and safety of consumers. However, there is no current legal definition for the ''gluten-free'' claim in the United States (U.S.) (Ref. 1). This lack of a definition prevents market and legal mechanisms from working effectively.

Currently, approximately 5% of foods labeled "gluten-free" do not meet the definition for "gluten-free" in this final rule (Ref. 5). As we show below in the Detailed Analysis, this means that about 19,000 individuals diagnosed with celiac disease consume such foods daily and are at risk of harm due to a 50 mg daily gluten intake from such food represented to be "gluten-free." We use the term "harm" in this analysis to reflect the morphological damage that 50 mg of gluten per day has been shown to cause in those with celiac disease (Ref. 6). This rule will

reduce that morphological damage by enabling market and legal mechanisms to operate more effectively.

Without a legal definition, consumers are less able to differentiate among GF labeled foods. This rule defines when a GF claim can be made in food. This means that consumers can accurately identify products that meet Federal definition of “gluten-free” and avoid comparable products that do not meet the definition and thus cannot be labeled as “gluten-free.”

C. Analysis of Regulatory Alternatives

The final rule prohibits the use of the "gluten-free" label in foods that contain 20 or more parts per million (ppm) gluten, and also prohibits the GF claim on foods that have any quantity of certain ingredients. If a food contains wheat, rye, barley, or their crossbred hybrids, it cannot be labeled "gluten-free". If a food has any ingredient derived from those grains, it cannot be labeled GF unless those ingredients have been specially processed to remove gluten. Additionally, a food labeled GF and that also bears the term "wheat" in its ingredient list or has a "contains wheat" statement in its labeling under section 403(w) of the FD&C Act must also bear additional language to clarifying that the food complies with FDA requirements for a "gluten-free" claim. The rule also requires that when the claims "no gluten," "free of gluten," and "without gluten" are made on a food, that food must meet the definition for "gluten-free" in this rule.

The final rule states that the FDA will enforce the <20 ppm part of the definition using a scientifically valid method that can reliably detect the presence of 20 ppm gluten in a variety of food matrices. Currently, there is no test method that can quantify the amount of gluten in foods that have been fermented or hydrolyzed, which means that the FDA does not have the ability to test such foods to determine their compliance. We intend to publish a proposed rule addressing how we will evaluate compliance with this rule when an evaluation of compliance based on an analysis of the food using a scientifically valid method is not available because the food is fermented or hydrolyzed or contains fermented or hydrolyzed ingredients. For the purposes of this economic analysis, to avoid double counting, we assume that this final rule will not cause any changes to foods that are or contain ingredients that are fermented or hydrolyzed because we attribute changes in these products to the proposed rule, as described in the regulatory impact analysis for the proposed rule.

We have identified eight regulatory alternatives:

1. Take no action;

2. The final rule;

3. The final rule, with the additional restriction that inherently gluten-free foods may only bear a "gluten-free" label if they have an additional disclaimer saying that all foods of the type are also gluten-free;

4. The final rule, but with the 20 ppm limit replaced with some other number;

5. Defining "gluten-free" as having less than 20 ppm gluten, with no restrictions on ingredients;

6. The final rule, but with an additional definition of the term "low gluten";

7. The final rule, but defining oats as an additional gluten-containing grain; and

8. The final rule, but with the compliance date set at January 1, 2016.

1. Take No Action

The baseline for this regulatory analysis is the continued lack of a definition for "gluten-free" claim on the labeling of food. We assume that, in the absence of any rule, conditions in the future will be similar to the conditions we currently observe. We believe that current conditions are causing harm to individuals with celiac disease that can be avoided at relatively low cost, as we show below in the Detailed Analysis.

2. The Final Rule

The benefits of this final rule are health gains for people currently consuming foods labeled "gluten-free", and reductions in search costs for people who start trusting and using the "gluten-free" label. All numbers in this section are summary estimates for mean parameter values; for explanation and an analysis of uncertainty, see the Detailed Analysis.

We found health gains by estimating the current harm being done by foods not complying with this final rule, and comparing that to the harm that would be done if all covered foods met the definition. We estimate that about 19,000 individuals diagnosed with celiac disease are being exposed to more than 50 mg of gluten daily because of foods carrying the "gluten free" label that are above 20 ppm gluten, and that this exposure results in the loss of 665 quality adjusted life years (QALYs) a year, generating a social cost of about $146 million. If all foods without

fermented or hydrolyzed ingredients met the regulatory definition, then the QALY loss would drop to 164 a year and the social cost would be reduced to $36 million.[1] Therefore, we estimate that the rule will save 501 QALYs a year (665-164=501), generating annual health benefits valued at $110 million (146-36=110).

As described in the Preliminary Regulatory Impact Analysis, when it becomes public knowledge that foods labeled "gluten-free" meet a common definition, people with celiac disease will be more likely to consume foods labeled GF rather than spending time researching their diet. This reduction in search costs will also improve the social welfare of people with celiac disease, as discussed in the Preliminary Regulatory Impact Analysis, but we do not have enough information to accurately quantify the benefits.

According to the midpoint estimate of the FDA's labeling cost model, relabeling foods that are currently labeled as "gluten-free" that do not comply with this final rule will require a one-time cost of $7.1 million. We annualize this cost over ten years using a cost of capital of 7% to estimate that the rule will cost approximately $1 million per year due to label changes.[2]

The cost of the rule is the required relabeling of foods that do not comply with the rule. Although the rule does not require testing, some producers of "gluten free" foods may choose to perform additional testing to learn the gluten content of their food. We estimate the costs of this testing.

Testing involves up-front costs such as sending samples to a lab and training workers to use test kits, and recurring costs such as regular use of test kits and annual lab tests. We estimate that the annualized cost of testing foods that are not currently being tested will be $5.8 million with a 7% cost of capital.[3]

Subtracting the costs from the benefits yields an expected net benefit of over $103 million per year. This large difference between benefits and costs is due to the fact that a small

[1] After the proposed rule regarding GF claims on hydrolyzed and fermented food is finalized and the compliance date is in effect, if all foods complied with the requirements in these rules, then the average diet composed of foods labeled GF would have 12 mg of gluten daily and all QALY loss from more than 50 mg of gluten daily in such diets would be eliminated.
[2] With a cost of capital of 3%, the annualized cost of relabeling is $0.8 million.
[3] With a cost of capital of 3%, the annualized cost of testing is $5.1 million.

number of foods carrying the "gluten free" label that are above 20 ppm gluten are causing morphological damage to individuals with celiac disease.

Table 1.—Annual Benefit and Cost Overview

Benefits	Health Gains for Individuals with Celiac Disease	$ 110,000,000
	Search Cost Reduction	Unknown
Costs	Relabeling of Foods	$ 1,000,000
	Voluntary Testing of Foods	$ 5,800,000
Net Benefits		> $ 103,000,000

3. Inherently Gluten-Free Foods Label Restriction

We considered the alternative of adding an additional restriction. This alternative would have prevented producers from putting a GF label on foods that were inherently free of gluten, with the exceptions of grains, legumes, and seeds, unless they included an additional disclaimer saying that all foods of the type are also gluten-free. This alternative would have all of the costs and benefits of the final rule, as well as additional costs and benefits:

The additional benefit of this alternative is that it would eliminate socially wasteful attempts to take money from uninformed consumers. Society is harmed by a "gluten-free" claim on an inherently gluten-free food if the product with the claim is identical[4] to the competitors' products, and consumers believe that the product with the claim is different, and they stop buying the competitors' products based on this false belief.

The transfer of money from consumers and competitors to the company making the claim should not be considered a social loss. The resources that the company spent changing the package and making the label are an economic loss. Option 3 would prevent these wasteful label changes in the future. We do not have enough information to quantify this benefit of Option 3, because we do not know how many label changes will happen.

[4] 'Identical' means no difference in gluten content.

Furthermore, if individuals with celiac disease were previously buying competitors' unlabeled products, and the GF label on other products that are identical to the competitors' products causes individuals to believe that the products without the GF labeling are not gluten free and should be avoided, then they might stop consuming that product rather than switch brands. This would reduce their enjoyment of their diet, and may cause them to abandon a GF diet and suffer negative health effects. Option 3 would eliminate this possibility.

In summary, the additional benefits of this alternative are a reduction in socially wasteful expenditures on label changes, and a reduction in the chances of misinformed consumers with celiac disease making harmful changes to their diets.

An additional cost of this alternative is that it would prohibit companies from using an unqualified GF label when they have made efforts to prevent gluten cross-contact. Several years ago, only oats were recognized in the scientific literature as subject to cross-contact with gluten-containing grains due to the conditions of their growing, handling, and processing. Since then, many other foods have been identified that can be subject to cross-contact with gluten (Ref. 5).

In the future, new foods in addition to grains, legumes, and seeds may be identified that are subject to cross-contact but are not exempted from the labeling rules in this alternative, and companies would have reduced incentives to prevent this cross-contact. They would not be able to advertise their food as gluten free, without making a potentially inaccurate and misleading claim about competitors' products.

If it is found that a food, not exempted in the alternative, often contains gluten due to cross-contact, then individuals with celiac disease would either continue to suffer health consequences due to gluten, or drop the foods from their diet and reduce their quality of life, or incur search costs to identify the brands that do not contain gluten due to cross contact.

Another cost of the alternative is the possible misinterpretation of the labels required by this alternative. A statement that all foods of that type are GF might cause individuals with celiac disease to buy a similar mixed or processed food that is not GF. For example, after seeing a rice product that states "rice, a gluten-free food," a consumer may mistakenly buy a rice pilaf product that happens to contain gluten, thinking that it would also be gluten-free.

In summary, the costs of this regulatory alternative are a reduction in company incentives to prevent cross-contact of inherently gluten free foods and possible misinterpretation of labels. Both of these effects could introduce harmful amounts of gluten into the diets of people with celiac disease.

Because of the many potentially relatively large costs of Option 3, and the uncertain, but small amount of potential benefits, we believe that the net benefits of this regulatory alternative are lower than the net benefits of our final rule.

4. Limit Other Than 20 ppm

We also considered, as a criterion for gluten free labeling, precluding the use of such labeling on foods with other levels of gluten content than what is required in this final rule. However, we have chosen to analyze alternative levels higher than 20 ppm gluten because we do not know of any currently available and appropriate test methods that can reliably and consistently detect gluten in a variety of food matrices at levels below 20 ppm.

Setting the threshold level of gluten in a food greater than 20 ppm would potentially lower the health benefits from the rule. For example, if GF labeled foods had a gluten content distributed uniformly between 0 and 50 ppm, then the simulation model described in the Detailed Analysis shows that 5.2% of GF diets would contain more than 50 mg of gluten daily, causing a QALY loss similar to the baseline and greatly reducing the health benefits of the rule. Therefore, we believe that the net benefits of this regulatory alternative are lower than the net benefits of our final rule.

5. Allowing Gluten-Containing Ingredients

This regulatory alternative would allow the use of gluten-containing grains or ingredients derived from them in GF food, as long as the concentration of gluten in the final product was below 20 ppm. The benefit of this alternative is increased dietary options for individuals with celiac disease. The cost of this alternative is an increase in number of “gluten-free” products with “contains wheat” statements or wheat in the ingredients list and potential for reduced confidence in the rule among individuals with celiac disease, which would increase their search costs.

We found a small number of foods[5], usually made with wheat-containing soy sauce, which carried a GF claim and probably contain less than 20 ppm gluten. Our final rule will require companies to remove the GF label from these foods, which will cause a small reduction in the dietary options of consumers currently consuming food bearing GF labels, and this alternative would have reduced that cost.

A proliferation of "gluten-free" products with wheat could cause consumers to mistrust the label, even with a required disclaimer. As we describe in the Detailed Analysis, there are an estimated 292,000 individuals with celiac disease complying with a gluten-free diet. For example, as a low estimate, if 10% of them stopped trusting the GF label as a result of this alternative, and started to read ingredient lists looking for gluten-containing ingredients, then the time it takes for them to shop would increase by 0 to 18 minutes a week, for an average time cost of $240 per week. This means that their total search costs would increase by $7 million a year (292,000 x 0.1 x 240 = 7,008,000).

We believe that any additional benefits of this regulatory alternative are lower than the associated increased search costs, which means that the net benefits of this alternative are likely to be lower than the net benefits of our final rule.

6. Defining "Low Gluten"

In addition to defining "gluten-free," we could have defined the food labeling claim "low gluten" to indicate foods that met a less strict definition. We believe that the benefits of this would have been very low. We were not able to find many products labeled "low gluten" in countries where this claim is allowed.[6] This suggests that there is very little consumer demand for such products in those countries, or that the costs of improving food from a "low gluten" definition to a "gluten-free" definition are very low. We have no evidence that suggests that individuals in the U.S. with celiac disease would desire such foods more than individuals with celiac disease in other countries.

[5] Using the FoodEssentials database (Ref. 20)
[6] We searched the FoodEssentials database for any foods with a 'low gluten' claim, and we searched online stores such as amazon.co.uk and tesco.com for any products with a 'low gluten' claim. We did not find any products that had a "low gluten" claim but not a "gluten-free" claim.

The addition of alternate definitions would have increased search costs for consumers, and testing costs to determine compliance with variable definition (low- and no-gluten) due to the additional complexity of information presented in the rule. If individuals with celiac disease are presented with a more complex rule, and they may not trust it or spend the time to learn it, they will continue shopping as before. This would potentially reduce or eliminate the social gains from more people using GF labels.

7. Prohibiting Oats

This regulatory alternative would prohibit food containing oats from being labeled as "gluten-free." The benefit of this regulatory alternative would be reduced search costs for the minority of people on a gluten-free diet who also suffer harm from eating oats. Estimates suggest that less than 9% of people on a gluten-free diet are allergic or intolerant to oats (Ref. 7). The cost of this regulatory alternative would be reduced dietary options for the majority of individuals with celiac disease, who can tolerate oats and who use oats as a replacement for the grains they can no longer consume.

Oats may contain gluten if they are processed in facilities that also process gluten-containing grains and sufficient controls are not in place to prevent cross contact. However, as discussed in Response 9 of the Preamble, oats themselves are inherently gluten free and can be processed in a way that protects against such cross-contact. Many people on a gluten-free diet benefit from gluten-free oats that have been processed to avoid cross-contact, or foods made with such oats as an ingredient. If companies were not allowed to label oats or oat-containing foods as "gluten-free", then they would have weaker incentives to keep gluten levels low in those foods, which could harm certain oat-tolerant gluten-free consumers. These individuals with celiac disease would have to choose between consuming no oats and paying large search costs to find safe oats.

Almost all sources of oats in food are listed with the word "oat" in the ingredient list, and there are private gluten-free certification programs that prohibit oats (Ref. 8). The search costs for the oat-intolerant group under the final rule are small, compared to the search costs for the oat-tolerant group under this regulatory alternative.

8. January 2016 Compliance

This regulatory alternative would change the compliance date to January 1, 2016, from one year after the publication of the rule. This alternative would lower compliance costs. We estimate that giving producers an additional 18 months would change the one-time cost of labeling to about $1.5 million, from about $7.1 million, generating a cost savings of about $5.6 million (7.1-1.5=5.6). The lack of testing for those 18 months would generate an additional $8.7 million in cost savings ($5.8 million annual costs x 1.5 = $8.7 million), bringing the total one-time savings to $14.3 million (5.6+8.7=14.3).

This regulatory alternative would also decrease the benefits, resulting in 18 months of illness that could be prevented by the rule. We estimate that this rule will generate health benefits of $110 million a year, meaning that delaying the rule by 1.5 years will cause a health loss of $165 million (110x1.5=165). Therefore, we conclude that the net benefits of this alternative are lower than the rule.

D. Benefits and Costs of the Final Rule: Detailed Analysis

There is a large degree of uncertainty inherent in this estimation. Each number we use in the calculations is uncertain, with the exception of the U.S. population. To reflect this uncertainty, we define all inputs as probability distributions. In this section, we illustrate the analysis with the mean value of each probability distribution. In the Analysis of Uncertainty, we generate low and high estimates with a Monte Carlo simulation that draws values at random from the probability distributions.

For many parameters, we have a low estimate, a high estimate, and a best estimate. In this case, we draw the parameter from a triangular distribution. The low estimate is the minimum value of the distribution, the best estimate is the peak of the distribution, and the high estimate is the maximum value of the distribution. The mean of a triangular distribution is the average of the three estimates used to generate the distribution.

All numbers are rounded to three significant figures, for presentation and to avoid false precision.

1. Benefits of the Final Rule

In order to find the benefits of the rule, we estimate the harm done by dietary gluten intake from a "gluten-free" diet before and after the rule. We find the number of people harmed under the baseline and the amount by which they are harmed.

a. Number of Individuals with Celiac Disease on a Gluten-Free Diet

According to the most recent National Health and Nutrition Examination Survey (NHANES) survey of the civilian non-institutionalized population of the U.S. (Ref. 9), 14 out of 10,107 people, or 0.14% (14/10,107 = 0.138%) have been told by a medical professional that they have celiac disease[7]. The most recent census estimate of the civilian non-institutionalized population is about 307 million, so we multiply the population by the percentage of individuals with celiac disease to estimate that there are about 430,000 people diagnosed with celiac disease in the U.S. (307,000,000 x 0.14% = 429,800).

This estimate does not include people who choose to remain on a gluten-free diet for reasons other than medically diagnosed celiac disease. There are also many individuals with celiac disease without a medical diagnosis of celiac disease. Many of these people may have self-diagnosed and chosen to eat a gluten-free diet, which means that they will also benefit from the rule. We do not have enough data to include them in the core analysis, but in the Other Potential Benefits section, we discuss how the benefits of the rule increase if they are included.

We do not know the harm that is caused by foods carrying the "gluten free" label that are above 20 ppm gluten in individuals with celiac disease who are only partially compliant with the gluten-free diet, so we must exclude them from the analysis. There have been many estimates of the percentage of individuals with celiac disease who comply with the gluten-free diet. The estimates of compliance range from 45% to 80%. The best estimate is a 2008 study where nutritionists interviewed the patients and determined that about 79% had good or excellent adherence with a gluten-free diet, meaning that they knowingly eat gluten once a month or less (Ref. 10).

[7] Only one year of NHANES survey data is available for the percentage of the population with doctor-diagnosed celiac disease, and one year of NHANES data should not be considered a nationally representative sample. In the Analysis of Uncertainty, we show how we generated a probability distribution to reflect this uncertainty.

We therefore use a triangular distribution with minimum 45%, maximum 80%, and a peak of 79%. This yields an estimated average of 68% compliance ([45+80+79]/3 = 68). Multiplying this percentage by the number of individuals diagnosed with celiac disease, we find that there are approximately 292,000 individuals diagnosed with celiac disease complying with a gluten-free diet (430,000 x 68% = 292,400).

b. Estimating Baseline Gluten Consumption

To estimate the baseline gluten intake, we use gluten testing results of food currently labeled "gluten-free" and data on diets from the NHANES survey (Ref. 11), to simulate gluten-free diets and the daily gluten intake from those diets. These simulated diets consisted of a random selection from the list of tested GF foods and from inherently gluten-free foods, in random amounts matching the observed distribution of serving sizes.

Comments from the Celiac Sprue Association (Ref. 5) included test results for 1000 food products labeled "gluten-free." The amount of gluten detected, if any, was reported for each individual food. Of these, 49 had levels of gluten above 20 ppm. This is the best source of data we have of foods labeled GF, and it is reasonable to assume that it is a representative sample of all GF foods. The data included a wide variety of foods, including baked goods, dried fruit and nuts, flours, frozen entrees, gravies, meat, and soup mixes. Other studies (Refs. 12, 13) have reported a slightly larger percentage of foods whose gluten content exceeds the limit in this final rule, but they were not as comprehensive and did not report data for individual food products.

The NHANES Total Nutrient Intakes tables show that the average consumer consumed 15 servings of food and drink daily. The NHANES Individual Foods data show the grams of each food or beverage serving that was consumed. Serving sizes of beverages are larger than serving sizes of foods, and there were many outliers of very large serving sizes from beverages. Beverages are rarely a source of gluten. Using the serving sizes of both foods and beverages to estimate the distribution of serving sizes of "gluten-free" food would have caused the serving sizes to be biased upwards, which would cause us to overestimate the gluten intake. Therefore,

we removed water, beverages, juices, milk, and raw watermelon from the data, which resulted in a mean serving size of about 82 grams. We then fit a gamma distribution to these values.[8]

We then simulated 100,000 gluten-free diets. Each diet consisted of a mix of inherently gluten-free foods and the tested "gluten-free" foods. We do not know what proportion of the average gluten-free diet comes from inherently gluten-free foods and foods labeled GF, but we do know that some consumers mainly rely on their own research of safe foods and others purchase products with GF labels almost exclusively. We therefore drew the proportion of labeled food in each diet from a uniform distribution with a minimum of 0 and a maximum of 1. Each diet consisted of 15 random draws of an inherently gluten-free food, or from one of the 1000 tested foods, according to that diet's proportion of labeled foods. The amount of each food eaten was drawn from the previously defined gamma distribution.

For foods where there was no detectable gluten, or about 89% of all tested foods, we assumed zero gluten. We also assumed zero gluten from inherently gluten-free food and from other sources. Changing this assumption to add trace amounts of gluten from these foods or other sources would have increased the percentage of diets that contained more than 50 mg of gluten. This would have inflated the estimate of the number of people harmed at the baseline, and the benefits of the regulation.

The highest amount of gluten that can be safely consumed each day by individuals with celiac disease is not known, and is likely to vary from person to person. We choose a threshold value for harm of 50 mg of gluten per day because this amount has been shown to cause morphological damage to most individuals with celiac disease in a double-blind, placebo-controlled challenge study (Ref. 6). This choice underestimates the true benefits of the rule, because it underestimates the baseline harm. As we explain in the Other Potential Benefits section, individuals with celiac disease are probably harmed by consuming smaller amounts of gluten daily, and this rule will also reduce intake at those levels.

[8] The gamma distribution was chosen because the data were extremely right-skewed, with many small values but no negative values, and the gamma distribution is flexible enough to fit such data without truncation. We found that the distribution of food serving sizes had a shape parameter of approximately 0.86 and a scale parameter of approximately 95.

The simulation results in roughly 6.5% of the simulated diets containing more than 50 mg of gluten. This result is not significantly affected by our choice of the gamma distribution to model the amount of each food consumed. A simulation where people consumed exactly 82 grams of all foods resulted in about 7.7% of diets containing more than 50 mg of gluten. We choose the gamma-distribution simulation because it is a more accurate model and it avoids overestimating the benefits of the rule.

We multiply the estimate of the percentage of gluten-free diets with 50 mg or more of gluten by the number of individuals with celiac disease on a gluten-free diet to produce an estimate of approximately 19,000 individuals with celiac disease harmed by 50 mg or more of gluten in foods labeled "gluten-free" (6.5% x 292,000= 18,980).

c. QALY Loss from Baseline Consumption and Social Cost

Our approach to estimating the benefits of being in good health (health benefits) involves the use of Quality-Adjusted Life Years (QALYs). QALYs can be used to measure the loss of well-being that an individual suffers due to a disease or condition. The QALY calculation does not include the cost of medical expenditures caused by the illness in question. QALYs range from 0 to 1, where 0 is equivalent to death and 1 is equivalent to perfect health for one year.

A number of methods have been constructed to measure QALYs. The studies that we reference use the EQ-5D health index to calculate changes in QALY as a result of celiac disease. The EQ-5D index allows us to estimate an individual's disutility from being ill in terms of the number of QALYs lost due to that illness. As shown in Table 2, the EQ-5D scale consists of five domains, with 3 levels for each domain, that assess an individual's mobility, ability to perform self-care activities, ability to perform usual activities (such as going to work or school), level of pain and discomfort, and level of anxiety and depression as a result of their medical condition.

Table 2.—EQ5D Health Status Classification System

Domain	Attribute Level	Description
Mobility	1	I have no problems walking about
	2	I have some problems walking about
	3	I am confined to bed
Self-Care	1	I have no problems with self-care

	2	I have some problems washing or dressing myself
	3	I am unable to wash or dress myself
Usual Activities	1	I have no problems with performing my usual activities
	2	I have some problems with performing my usual activities
	3	I am unable to perform my usual activities
Pain/Discomfort	1	I have no pain or discomfort
	2	I have moderate pain or discomfort
	3	I have extreme pain or discomfort
Anxiety/Depression	1	I am not anxious or depressed
	2	I am moderately anxious or depressed
	3	I am extremely anxious or depressed

We found three articles that reported EQ-5D scores for treated and untreated individuals with celiac disease (Refs. 14-16). The reported increases as a result of treatment were 0.20, 0.21, and 0.27. Given that treatment for celiac disease is the removal of gluten from the diet, we conclude that exposing an individual with celiac disease to the levels of gluten in the average diet results in a mean QALY loss of 0.23 ([0.2+0.21+0.27]/3 = 0.227).

We do not have dose-response relationships for gluten in people with celiac disease, so we do not know how the QALY loss that such individuals experience from consuming 50 mg of gluten daily compares with the QALY loss from consuming a normal diet. There is no research that defines the distribution of gluten sensitivity across the population, so we are forced to make estimations based on averages from small and limited studies.

The morphological changes caused by 50 mg of gluten per day over 90 days were measured and reported by analyzing the geometry of an intestinal villi biopsy. (Ref. 6) The observed reduction in villi at the end of 90 days was about 5% of the damage that is observed in patients who have had untreated celiac disease for years. We do not know if consuming 50 mg of gluten daily for longer periods would cause even more deterioration, or if the villi would stabilize at the observed level. Although it is likely that more time would cause more deterioration, we use this study to generate a low estimate that 50 mg of gluten causes 5% of the harm a normal diet would cause.

A study (Ref. 15) found that the difference in EQ-5D score between people with good compliance and people with inadvertent partial compliance with the gluten-free diet was 0.13. Inadvertent partial compliance was defined as patients reporting that they sometimes forget about the diet or do not comply carefully with it. Patients with good compliance improved EQ-5D by 0.28 and patients with partial compliance improved ED-5D by 0.15, meaning that partial compliance causes 46% of the damage caused by a normal diet (0.13/0.28=0.46) We adjust this estimate downward, based on the margins of error presented in the study, to avoid overstating benefits, and to reflect the fact that a constant small dose of gluten may do less damage than occasional large doses, and generate a high estimate that 50 mg of gluten causes 30% of the harm a normal diet would cause.

We have a study showing that prolonged exposure to amounts of gluten smaller than 50 mg daily causes individuals with celiac disease to report symptoms that lower their quality of life (Ref. 17). The symptoms reported correspond to ICD-9 code 536, Stomach Function Disorders, which has an average disutility of 0.0228 on the EQ-5D scale (Ref. 18), so we use these studies to generate a best estimate that 50 mg of gluten causes 10% of the harm a normal diet would cause.

The mean of the triangular distribution generated by these estimates is 15%. ([5+10+30]/3 = 15) This means that, on average, an individual with celiac disease who consumes more than 50 mg of gluten daily as a result of exposure to gluten from foods carrying the “gluten free” label that are above 20 ppm gluten suffers a QALY loss of 0.035 (0.23 x 15% = 0.0345).

Multiplying the estimate of the number of individuals with celiac disease harmed by the estimate of the QALY loss of the harm produces an estimate of approximately 665 QALYs lost each year from diets that have more than 50 mg of gluten daily as a result of consuming “gluten-free” food with levels of gluten of 20 ppm or higher (19,000 x 0.035 = 665).

We use the Value of a Statistical Life Year (VSLY) to convert QALY benefits to dollar benefits. We repeat our analysis with three different VSLY values, to reflect the uncertainty in the literature on valuation. The VSLY values we use are $109,813; $219,626; and $329,439 in 2011 dollars, based on VSLY and Cost Effectiveness Analysis literature which often cites $100,000, $200,000 and $300,000 as values (base year 2006) (Ref. 19).

Using the middle value of a VSLY, the current social loss from food labeled "gluten-free" with 20 ppm or more gluten is approximately $146 million annually. (665 x $219,626 = $146,051,290) Using the low value, the harm is approximately $73 million annually (665 x $109,813 = $73,025,645). Using the high value, the harm is approximately $219 million annually (665 x $329,439 = $219,076,935).

Table 3 summarizes the variables and the results of the calculations explained above, using mean values for all variables:

Table 3.—Baseline Harm Calculation Summary

Variable	Mean Value
Non-institutionalized Civilian Population	307,000,000
Percent of Population Diagnosed with Celiac Disease (CD)	0.14%
Individuals Diagnosed with CD	430,000
Percent of CD-Diagnosed Individuals on GF Diet	68%
CD-Diagnosed Individuals on GF Diet	292,000
Percent of GF Diets Above 50 mg	6.5%
CD-Diagnosed Individuals on GF Diet Consuming >50 mg of gluten	19,000
QALY Loss for Untreated Celiac Disease	0.23
Severity of 50 mg Compared to Untreated	15%
QALY Loss for >50 mg of gluten	0.035
Annual QALY Loss from High-gluten Food	665
Cost per QALY	$ 220,000
Total Annual Baseline Harm	$ 146,000,000

d. Gluten Consumption with Rule

Next, we simulated gluten-free diets after introduction of the final rule. We assumed full compliance with the rule for all foods that the FDA can test, meaning that no testable food with a voluntary "gluten-free" label has any of the characteristics that would cause it to be misbranded under this rule. However, we assume that the rule would not affect fermented and hydrolyzed

foods or foods with those ingredients because those effects are taken into account in the separate proposed rule regarding how FDA will evaluate compliance for fermented or hydrolyzed foods.

As in the previous simulation, all diets consist of a mix of inherently gluten-free foods and foods with a "gluten-free" label. When a high-gluten food with a "gluten-free" label is removed from the market, the consumer replaces the food with either a different gluten-free brand of the food product, or a different type of gluten-free food.

We searched the FoodEssentials database (Ref. 20), a comprehensive survey of food products sold nationwide in the U.S., for foods with claims about gluten that would be affected by the final rule: "gluten-free", "no gluten", "free of gluten" and "without gluten." The search also included variations of these claims within larger sentences, such as "No milk, soy, or gluten." We refer to all such claims as "gluten-free" claims. We found 11,108 such foods.

We then searched the foods with "gluten-free" claims for ingredients that are fermented or hydrolyzed. For the purposes of this search, we considered autolyzed yeast extract to be a hydrolyzed food, based on 21 CFR 102.22. We searched for foods with one or more of the following words in the ingredients list: hydrolyzed, autolyzed, yeast extract, fermented, beer, brandy, cheese, cider, fish sauce, kimchi, kombucha, miso, pepperoni, pickle, salami, sauerkraut, vinegar, vodka, whisky, wine, and yogurt. We found 2,514 such foods, which means that approximately 23% of all foods with a "gluten-free" claim are or contain one or more ingredients that are fermented or hydrolyzed (2514/11108 = 0.226).

We assumed the unlikely worst-case scenario where all "gluten-free" products covered by the rule contain up to 19.9 ppm gluten (uniform distribution between 0 and 19.9) and all fermented and hydrolyzed foods had the same distribution of gluten content as the 1000 tested foods used in the initial simulation. We assumed that 23% of all labeled "gluten-free" foods consumed are fermented and hydrolyzed. In all other respects, the simulation of diets after the rule was the same as the simulation of diets before the rule.

This second simulation results in roughly 1.6% of the simulated diets containing more than 50 mg of gluten. Replacing 6.5% with 1.6% in the harm calculation described above yields an estimated annual harm of 164 QALYs, which is valued at $36 million. The difference between the values before and after the rule, 501 QALYs or $110 million, is the estimated health

benefits that Americans with celiac disease who are following a gluten-free diet will enjoy due to the final rule.

e. Search Cost Reduction

The Preliminary Regulatory Impact Analysis found that the ability to rely on "gluten-free" labels would save consumers between 0 and 18 minutes per week when shopping for groceries. This means that the average consumer of "gluten-free" food would save between $0 and $480 per year, or an average of $240 per year, in search costs as a result of using labels. According to the Preliminary Regulatory Impact Analysis, the annual value of benefits will be $240, times the number of consumers who will start trusting the "gluten-free" label as a result of the publication of the final rule.

While it is not possible to accurately quantify the search cost reductions as a result of increased trust in the GF label, we can generate a rough estimate. As described above, there are 292,000 individuals with celiac disease complying with a gluten-free diet. Some of them currently rely mainly on their own research rather than GF labels. If 20% of individuals with celiac disease start trusting labels, and the time it takes for them to shop decreases by 18 minutes a week as described in the Preliminary Regulatory Impact Analysis, then their total search costs could decrease by $14 million a year. (292,000 x 0.2 x 240 = 14,016,000) These savings are a potential additional benefit of the rule.

f. Other Potential Benefits

NHANES survey data (Ref. 9) show that 0.62% of the civilian non-institutionalized population of the U.S. is on a gluten-free diet. We believe that many of these people have undiagnosed celiac disease, and gain the same benefit from a gluten-free diet as do individuals diagnosed with celiac disease. The estimated prevalence of celiac disease in the U.S. population, including both diagnosed and undiagnosed individuals, is 1 in 133, or 0.753% (Ref. 21), which means that there are many undiagnosed individuals with celiac disease in the population.

Individuals with undiagnosed celiac disease on a gluten-free diet would suffer the same harm from foods carrying the "gluten free" label that are above 20 ppm gluten as individuals with diagnosed celiac disease. We do not count these undiagnosed people in the analysis,

because we do not know how many people on a gluten-free diet actually have celiac disease and how closely they comply with the diet. It is possible that a significant percentage of people on a gluten-free diet are individuals with undiagnosed celiac disease who have good compliance with the diet. If this were the case, then the harm done by foods carrying the "gluten free" label that are above 20 ppm gluten would be much greater than we estimate, and the benefits of the rule would also be much greater.

Our benefit numbers are based on the estimate that 0.1% of the U.S. population consists of people with diagnosed celiac disease who comply with a gluten-free diet (0.14% x 68% = 0.0952%). If one-sixth of the people on a gluten-free diet were individuals with undiagnosed celiac disease with good compliance, then there would be an additional 0.1% of the population benefiting from the rule (0.62 / 6 = 0.103), meaning that the benefits of the rule would be double our estimates.

In addition to eliminating diets with more than 50 mg of gluten per day, the rule would reduce the percentage of diets with levels of gluten that might cause lesser harm. About 2.5% of simulated baseline gluten-free diets have between 20 mg and 50 mg of gluten per day. After the rule is in place, about 1.7% of diets have between 20 mg and 50 mg of gluten per day. If levels of gluten between 20 mg and 50 mg per day cause health problems for individuals with celiac disease, than those health problems will be reduced as a result of the rule.

The distribution of gluten in the simulated diets is extremely right-skewed. Over two-thirds of all diets with more than 50 mg of gluten per day had over 100 mg of gluten per day. In our analysis, we assumed that all simulated diets with more than 50 mg of gluten per day cause the same harm. If diets with larger amounts of gluten, such as 100 mg per day, cause substantially more harm, then the benefits of this rule will be larger than our estimates.

Untreated celiac disease can cause premature mortality in addition to losses in the quality of life (Ref. 2). We do not have any information on the mortality effects of smaller doses of gluten.

There are many people who choose a gluten-free diet for reasons other than celiac disease. For example, people who do not suffer from celiac disease but who are allergic to wheat often use the "gluten-free" label to quickly identify foods that are free from the wheat proteins

that trigger their allergic reactions. These people will also benefit from the rule. Anyone who is on a gluten-free diet for any reason will benefit from the reduction in search costs, if they start using and trusting the GF label as a result of this rule.

2. Costs of the Final Rule

For foods that are currently labeled as "gluten-free" but that do not meet the rule's definition, firms that incurred costs to add a "gluten-free" label prior to the publication of the final rule will incur similar costs in order to remove the claim. The potential costs of re-labeling include administrative, graphic, prepress, engraving and inventory costs to back panels and perhaps to front panels of the label. These costs vary based on the compliance date, the type of package that has to be changed, and how significantly the change alters the layout of the label.

Although the rule does not require testing, some producers may choose to perform additional testing to learn the gluten content of their food. Many producers currently test their products enough to ensure that the gluten content of their foods with a "gluten-free" claim is lower than 20 ppm, but some do not (Ref. 5). We estimate the costs of this additional testing.

Marketing and reformulation costs might be triggered by the rule, depending on the observability of the revoked claim among consumers and whether the market reverts to its pre-claim structure or moves to something completely different. We believe that removing the claim in response to this final rule will impose minimal, if any, reformulation costs because producers have alternate ways to market the product. The cheapest way to comply with the rule will be relabeling.[9] We consider the costs of the rule as those necessary to test for the presence of 20

[9] It is possible that producers may choose to start using an allergen control plan to eliminate gluten cross-contact, instead of relabeling. This would involve paying costs to change the production process, train workers, and possibly test ingredients and change suppliers. Producers may choose to pay these additional costs because the profits from doing so are higher than the profits from relabeling and abandoning the market for "gluten-free" labeled foods.

Elsewhere in this analysis, we do not count changes in consumer surplus from changing availability of "gluten-free" labeled foods, because there is no change in the availability of foods that are actually gluten-free. In this case, the availability could change. Relative to the baseline of a producer relabeling high-gluten foods and exiting the market for "gluten-free" labeled foods, changing the production to eliminate gluten cross-contact increases consumer surplus due to increased availability of gluten-free foods.

ppm or more gluten and to redesign and re-issue packaging and other labeling materials to remove the claim for foods that do not comply with this final rule.

a. Voluntary Testing Costs

Gluten testing can be done by sending product samples to a testing company, and by using test kits on site (Ref. 22). Test kits must first undergo method extension for the testing situation they are to be used in (Refs. 22, 23). We assume that a producer that begins a program of testing the gluten content of a product will start by sending several samples to a lab and obtaining method extension for a test kit for the product. This is a one-time cost.

After paying the startup cost, the producer will then use test kits to test their product on a regular basis, and may also send one or two product samples a year to an outside lab for testing. This is a recurring annual cost.

Testing companies charge between $68 and $110 per sample, with a best estimate of about $75 (Refs. 24, 25). The average of these estimates is about $84 ([68+75+110]/3 = 84.33), and we also estimate that producers will spend $26 per sample to collect the food and mail it to the lab[10], for a total cost per lab test of $110 (84.33+28=109.83).

Producers will test between 2 and 12 samples of each product or ingredient (Ref. 22), for an average of 7 samples and an average testing cost of $769 (109.83x7=768.83). Method extension costs between $1,000 and $10,000 with a most likely cost of $2,500 (Ref. 26), for an average cost of $4,500 ([1+2.5+10]/3=4.5).

This results in an average total one-time cost of $5,269 per product (769+4500 = 5269). We use Excel's PMT function to annualize this cost over ten years with a cost of capital of 7%

If a producer chooses to control gluten rather than relabel, then that must mean consumers are willing to pay at least as much as the cost difference. This means that total social surplus is higher from changing production than from relabeling. Therefore, the assumption of relabeling is a worst-case scenario, and changing it would increase the net benefits of the rule, but we do not have enough information to quantify this increase.

[10] A USPS Medium Flat Rate Box costs $12 and will hold most food samples. The cost of the food product or ingredient sent for testing will be about $10. Ten minutes of labor at $21 an hour will be required to mail the sample. 12+10+(21x10/60) = 25.5

and find that the annualized cost is $750 per year per product. If the cost of capital was 3%, the annualized cost would be approximately $618 per product.

Test kits cost about $11 each and take 10 minutes to use (Ref. 27). The average employer cost per hour worked in the manufacturing industry is $21 (Ref. 28) which means that the total cost of using a test kit is about $14.50 (11+[21x10/60]=14.5). We estimate that producers will use test kits between twice a year and once a week, with a best estimate of once a month (Ref. 26), per product. This yields an average of about 21 test kits used per year, at an annual cost of $309 per product (14.5x21.33=309.33). In addition to using test kits, companies will send between zero and two samples of each product or ingredient annually to an outside lab, for an average annual cost of $110. Adding up these two costs yields total recurring costs of $419 per product on average (309+110=419).

Adding the average recurring costs to the average annualized one-time costs yields total annual testing costs of $1,169 per product at a 7% cost of capital (750+419=1169) and $1,037 at a 3% cost of capital (618+419=1037) that can be attributed to this final rule.

We assume that all foods with a voluntary "gluten-free" label that do not contain fermented or hydrolyzed ingredients will be tested after the rule is in effect. According to our search of the FoodEssentials database (Ref. 20) described above, 8,594 food products in the database have a "gluten-free" claim and do not contain fermented or hydrolyzed ingredients. (11108-2514=8594). The additional testing costs that may happen as a result of this rule are based on the number of such foods not currently being tested.

The Gluten Intolerance Group's Gluten Free Certification Organization (GFCO) lists a product as "Certified Gluten-Free" after a facility audit and regular product testing (Ref. 29). We assume that producers of these food products, and producers of products tested by other certification programs, will not incur any additional testing or other costs as a result of this rule.

About 10,000 products are listed as "Certified Gluten-Free" by GFCO. Many of these are dietary supplements or ingredients that are only sold to other food producers. Many of the GFCO certified food products are from small specialty companies that are not listed in the FoodEssentials database.

Based on comparisons between the GFCO list and the FoodEssentials database, we estimate that at least half of all "gluten-free" consumer products are listed in the FoodEssentials database, meaning that there are no more than 17,000 "gluten-free" products affected by the rule.

We also estimate, based on our analysis of certification programs and manufacturer claims of testing independent of such programs, that at least half of all "gluten-free" products are already being tested for gluten. Therefore, we estimate that between 2000 and 8000 products currently labeled GF will be tested as a result of this rule.

With the average estimate of 5,000 products requiring testing, we estimate the total annual economic costs of testing that result from this rule to be about $5.8 million at a 7% cost of capital (1169x5000=5,846,000) and $5.2 million at a 3% cost of capital (1037x5000=5,184,000).

Table 4 summarizes the variables and the results of the calculations explained above, using mean values for all variables:

Table 4.—Testing Cost Summary

	Per Product	Total
Startup		
Initial tests	7	
Testing Cost	$ 769	
Method Extension	$ 4500	
Total One-time	$ 5,269	$ 26,300,000
Annualized		
3% Cost of Capital	$ 618	$ 3,100,000
7% Cost of Capital	$ 750	$ 3,800,000
Recurring		
Number of kits used	21	
Cost of Kits	$ 309	
Number of Lab Tests	1	
Cost of Lab Tests	$ 110	
Total Recurring	$ 419	$ 2,100,000

Total Annual Cost of Voluntary Testing: 3%	$ 1,037	$ 5,200,000
Total Annual Cost of Voluntary Testing: 7%	$ 1,169	$ 5,800,000

b. Voluntary Labeling Costs

We estimate that after products with a "gluten-free" label are tested and their ingredient lists examined, 5% of these foods will be found to need relabeling to comply with this final rule. This includes the 4.9% of foods with 20 ppm or more gluten and 0.1% with ingredients that do not satisfy the ingredient requirements in this final rule. This estimate of 0.1% is based on a search of ingredients of foods with a "gluten-free" claim in the FoodEssentials database.

We used the 2011 Labeling Cost Model (Ref. 30) to calculate the potential new labeling costs for those who chose to voluntarily label. The model calculates the cost of a new label based on the product type, label type, compliance time, and inflation. The compliance costs of labeling is lower if the required changes can be coordinated with planned label changes. Producers who chose to label will have 12 months from the date of publication to comply with the rule. The 2011 Labeling Cost Model uses a three to four year timeline for normally scheduled redesign, which means that most of the labeling changes required by this rule cannot be coordinated with planned labeling changes.

The costs per product of relabeling depend on the exact printing method, the amount of packaging in inventory, the labor costs of managing the relabeling process and other variable factors. Because these costs cannot be known with certainty, the Labeling Cost Model reports a low and high cost estimate for any required label change. The lowest estimated cost for relabeling during a 12 month compliance period is $3,414 per label for branded products, the highest estimated cost for a 12 month compliance period is $13,229 per label for private label products, and the estimated weighted average cost is about $7,101 per SKU.

According to the FoodEssentials database (Ref. 20), 8,594 of 271,872 products had a "gluten-free" claim that we estimate will be affected by this rule, so we estimate that 3.2% of all

foods have such a GF claim (8,594 / 271,872 = 3.2%). Because 5% of GF foods will have to be relabeled, we estimate that 0.16% of all foods will need to be relabeled (3.2% x 5% = 0.158%).

We entered this value of 0.16% of all foods requiring relabeling into the Labeling Cost Model, and the result was that it calculated relabeling costs for 1,096 products.

With a 12 month compliance period, the Labeling Cost Model estimates that 89% of branded product labels and 95% of private label product labels of labels using the claim will have to change their labels outside of the normal schedule. If 1,096 labels are affected, the rule will require 1,002 unscheduled label changes and 95 scheduled label changes. The average estimated label cost per product for a 12 month compliance period is $7,191 for unscheduled changes and $289 for scheduled changes. The higher cost reflects both discarded inventory and overtime or rushed order charges. The cost of relabeling due to the final rule is estimated to be approximately $7.1 million. This is a one-time cost. We use Excel's PMT function to annualize this cost over ten years with a cost of capital of 7% to estimate that the rule will cost approximately $1,016,000 per year due to label changes. If the cost of capital was 3%, the annualized cost would be approximately $837,000.

3. Total Costs and Benefits

The total annualized cost of the testing and relabeling is $6.9 million at a 7% cost of capital (5.85+1.02=6.87) and $6 million at a 3% cost of capital (5.18+0.83=6.01).

Subtracting the costs from the benefits yields a net benefit of over $103 million per year ($110- $6.9 = $103.1).

4. Analysis of Uncertainty

In Tables 3 and 4 of this document and elsewhere we present the expected effects of the final rule as point estimates. While this is a convenient way to summarize the effects of the rule and explain our calculation, the use of point estimates neglects the large degree of uncertainty intrinsic to the underlying analysis. In Table 5 of this document, we present the results of a Monte Carlo simulation of uncertainty for the eventual annual benefits and costs of the rule.

As we explained in the introduction to the Detailed Analysis, all parameters are defined as probability distributions. In our Monte Carlo simulation, we use samples from the probability distributions rather than using the mean values. The randomly chosen numbers are used to form a final estimate. This procedure is repeated 10,000 times, and the results are ranked from lowest to highest. We report the distribution for each input parameter, and the 5^{th} percentile, mean, and 95^{th} percentile of the simulated results.

We used an NHANES survey of 10,109 people to calculate that approximately 0.14% of the population has been diagnosed with celiac disease. When a sample of size 10,109 is drawn from a population of millions and yields 14 positive results, the standard error of that sample will be approximately 0.04% ((0.138% x 99.862% / 10,109) ^ 0.5 = 0.037%). Therefore we use a normal distribution with a mean of 0.138% and a standard deviation of 0.037%. We truncate this distribution at zero, because there cannot be a negative percentage of individuals with celiac disease. The 95% confidence interval of this distribution is (0.064%, 0.212%); the true prevalence of diagnosed celiac disease has a one in twenty chance of being outside this range.

As we described above, the estimate for compliance with a gluten-free diet is a triangular distribution with minimum 45%, peak 79%, and maximum 80%.

Our 100,000 simulations of the diets before and after the rule were split into ten simulation runs of 10,000 diets each. The percentage of diets with more than 50 mg of gluten before the rule varied from 6.2 to 6.8 across simulation runs, with most results clustered around 6.5. We describe this parameter as a triangular distribution with minimum 6.2%, peak 6.5%, and maximum 6.8%. The percentage of diets with more than 50 mg of gluten after the rule varied from 1.4 to 1.8 across simulation runs, with most results clustered around 1.6. We describe this parameter as a triangular distribution with minimum 1.4%, peak 1.6%, and maximum 1.8%

As described above, three estimates of QALY loss from untreated celiac disease are 0.20, 0.21, and 0.27. We draw the QALY loss from a triangular distribution with minimum 0.20, peak 0.21, and maximum 0.27. We draw the percentage harm that 50 mg of gluten causes compared to a normal diet from a triangular distribution with minimum 5%, peak 10%, and maximum 30%.

We drew the cost of lab tests from a triangular distribution with minimum $94, peak $101, and maximum $136, reflecting the sum of testing and handling costs. We drew the number

of products requiring new testing from a discrete uniform distribution with minimum 2000 and maximum 8000.

We drew the number lab tests ordered in the first year from a discrete uniform distribution with minimum 2 and maximum 12. We drew the cost of method extension from a triangular distribution with minimum $1,000, peak $2,500, and maximum $10,000.

We drew the annual number of test kits used per product from a triangular distribution with minimum 2, peak 12, and maximum 50. We drew the annual number of lab tests ordered from a discrete uniform distribution with minimum 0 and maximum 2.

The labeling cost model produced low, midpoint, and high estimates. Annualized at a 7% cost of capital, these are $0.58 million, $1.02 million, and $1.68 million, respectively. We drew labeling costs from a triangular distribution with low, peak, and high values equal to these low, mid, and high estimates.

We conducted separate simulation runs for the three estimates of a VSLY. Table 4 shows these results. The "Low" column shows the low estimates for the inputs and the 5th percentile of the simulation results. The "Mean" column shows the means for the inputs and simulation results[11]. The "High" column shows the high estimates for the inputs and the 95th percentile of the simulation results. All results are rounded to the nearest million for clarity and to prevent a false impression of precision.

We used a 7% cost of capital for all cost numbers.

Table 5.—Analysis of Uncertainty Summary

Variable	Low	Mean	High
Percent of Population Diagnosed with CD	0.064%	0.138%	0.212%
Percent of CD Diagnosed People on GF Diet	45%	69.7%	80%
Percent of GF Diets Above 50 mg Before Rule	6.2%	6.5%	6.8%
Percent of GF Diets Above 50 mg After Rule	1.4%	1.6%	1.8%
QALY Loss for Untreated Celiac Disease	0.2	0.227	0.27

[11] The mean of the simulation runs is slightly different from the calculation based on input means, because of rounding.

Average Severity of 50 mg Compared to Untreated	5%	15%	30%
Cost of Lab Test	$94	$101	$136
Products Requiring New Testing	2000	5000	8000
Initial Lab Tests	2	7	12
Method Extension Cost	$1000	$2500	$10000
Number of Test Kits Used Annually	2	21	50
Number of Annual Lab Tests	0	1	2
Annualized Relabeling Costs (Millions)	$0.58	$1.02	$1.68
Annual Net Benefits: $110k VSLY (Millions)	$12	$45	$94
Annual Net Benefits: $220k VSLY (Millions)	$32	$98	$196
Annual Net Benefits: $330k VSLY (Millions)	$53	$151	$298

For example, using the average ($219,626) estimate for a VSLY, there is a 5% chance that the annual net benefits of the rule are less than $32 million.

Because many uncertainties could not be measured, Table 4 should not be seen as a complete characterization of the uncertainty underlying the analysis. The net benefits could be larger than we report here, as discussed in the “Other Potential Benefits” section.

The biggest driver of uncertainty is likely to be the fact that there is a wide range of sensitivity to gluten among individuals with celiac disease. If each individual has a unique “dose-response” to gluten exposure, then there will also be individual variability with respect to QALY loss.

Regulatory Flexibility Analysis

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on a substantial number of small entities. We find that the impact of this rule is its requirement to change or withdraw "gluten-free" labels on products that do not satisfy the definition in this final rule, and the additional testing that may be required to identify such products. At least some of the affected products are produced by small businesses, and some small businesses may own multiple affected products. We estimate that the number of products that need to be changed under the final rule is approximately 1,096, but we do not know how many of them are owned by small businesses. The affected products will incur one-time costs of around $7,100 for relabeling and $5,300 for testing, for a total of $12,400 (7100+5300=12400).

Exempting small businesses from the rule may lift the burden on some small entities. However, because the potential harm done by foods with more than 20 ppm gluten is so large, and because exemptions would reduce public trust in the rule and cause consumers to incur search costs, such an exception would reduce or eliminate the benefits of the final rule.

Allowing small businesses more time for compliance may lift the burden on some small entities. However, because the potential annual harm done by foods with more than 20 ppm gluten is so large, and because exemptions during the transition period would reduce public trust in the rule and cause consumers to incur search costs, allowing more time for compliance for some producers would reduce the benefits of the final rule.

For example, if one-fourth of "gluten-free" products were produced by small businesses and exempted from the rule, then an additional 1.6% of simulated diets would contain more than 50 mg of gluten daily, resulting in an estimated annual harm of 164 QALYs or $36 million, compared to the baseline of full enforcement. This estimated loss to individuals with celiac disease is far larger than the estimated costs of complying with the rule.

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