DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Food Labeling; Gluten-Free Labeling of Fermented or Hydrolyzed Foods

Docket No. FDA-2014-N-0-1021

Preliminary Regulatory Impact Analysis

Preliminary Regulatory Flexibility Analysis

Preliminary Unfunded Mandates Reform Act Analysis

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A. Introduction

The Food and Drug Administration (FDA or we) has examined the impacts of the proposed 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 proposed rule is not an economically 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 proposed rule are small but not negligible, so we conclude that the proposed 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 $144 million, using the most current (2014) Implicit Price Deflator for the Gross Domestic Product. We do not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

We invite comments on this Preliminary Regulatory Impact Analysis.

B. Summary of Costs and Benefits

The proposed rule would establish requirements for the use of a "gluten-free" claim[1] in foods that are fermented or hydrolyzed or that contain a fermented or hydrolyzed ingredient, including that the manufacturer make and keep records providing adequate assurance that food is gluten-free before fermentation or hydrolysis, that the manufacturer has evaluated the potential for cross-contact with gluten during the manufacturing process, and, if necessary, measures are in place to prevent the introduction of gluten into the food during the manufacturing process.

The costs of this proposed rule, as discussed in further detail below, are estimated as the costs to test ingredients for gluten, evaluate potential for cross-contact, if necessary develop and carry out written standard operating procedures (SOPs) for preventing gluten cross-contact, relabel products that cannot be brought into compliance, and maintain records of these activities for FDA inspection. We estimate total annualized costs of $8.8 million at a 7% discount rate[2].

The benefits of this proposed rule are health gains for people using "gluten-free" labeled foods while maintaining a gluten-free diet. We found health gains by estimating the current harm being done by fermented and hydrolyzed foods not meeting the requirements in this proposed rule, and comparing that to the harm that would be done after the proposed rule (if finalized) removed these foods from the market for 'gluten-free' foods. We estimate that about 4,700 individuals diagnosed with celiac disease are being exposed to more than 50 mg of gluten daily[3] because of fermented and hydrolyzed foods carrying the "gluten free" label that are above 20 ppm gluten, and that this exposure results in the loss of 160 quality adjusted life years (QALYs) a year, generating a social cost of about $41 million. These estimates are for mean parameter values; for explanation and an analysis of uncertainty, see the Detailed Analysis.

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[1] The proposed rule also applies to the claims "no gluten," "free of gluten," and "without gluten." These claims are all considered to be "gluten-free" claims.

[2] At a 3% discount rate, annualized costs are $8.3 million

[3] 50 mg of gluten is the amount of gluten consumption that has been shown to cause morphological damage to most individuals with celiac disease. The mg amount of gluten consumed depends on the quantity of food consumed and its gluten concentration (measured in ppm). For example, eating 2500 grams of food with 20 ppm gluten would cause 50 mg of gluten to be consumed.

Subtracting the costs from the benefits yields an expected net benefit of about $32 million per year. This large ratio of benefits to costs is due to the fact that a small number of foods carrying the "gluten free" label that are above 20 ppm gluten are causing morphological damage to individuals with celiac disease, as we explain in the Detailed Analysis.

Table 1.—Annual Benefit and Cost Overview (USD Millions)

Costs	Testing of Foods	$ 3.0
	Standard Operating Procedure Development	$ 1.5
	Labeling	$ 0.3
	Paperwork	$ 3.9
Benefits	Health Gains for Individuals with Celiac Disease	$ 41
Net Benefits		$ 32[4]

[4] This number is rounded to the nearest million per the rules of significant figure arithmetic.

C. Need for Regulation

In the Federal Register of August 5, 2013 (78 FR 47154), we published a final rule that defines the term "gluten-free" and establishes requirements as to the voluntary use of that term in food labeling. The rule is codified at 21 CFR 101.91 (the gluten-free regulation). This proposed rule is a response to information asymmetries that arise due to limitations of analytical methods technology for enforcement of the gluten-free regulation when "gluten-free" claims are made about certain foods. The cost to most consumers of verifying that their food is gluten-free is higher than the private benefits, leading to a coordination problem that can be effectively solved by this regulation.

Gluten is a protein found in wheat, barley, rye, and their crossbred hybrids (Ref. 1). Wheat gluten is generally recognized as safe, (Ref. 2) and gluten-containing grains are staples in the food supply (Ref. 3). 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. 3).

People with celiac disease may be harmed by consuming gluten. The way for them to avoid harm is to maintain a gluten-free diet (Ref. 1). Many foods bear a "gluten-free" (GF) labeling claim to advertise that their food is safe for individuals with celiac disease.

The gluten-free regulation protects individuals with celiac disease by setting several requirements, one of which is that foods that bear a "gluten-free" labeling claim must have less than 20 parts per million (ppm) of gluten. The gluten-free regulation states that FDA will enforce the 20 ppm requirement using a valid test method that can reliably detect the presence of 20 ppm gluten in a variety of food matrices. Currently, there is uncertainty in interpreting the results of current gluten test methods for fermented and hydrolyzed foods on a quantitative basis that equates the test results in terms of intact gluten, which means that FDA does not have the ability to test such foods to determine their compliance.

Before the gluten-free regulation was published, approximately 5% of foods labeled "gluten-free" contained more than 20 ppm of gluten (Ref. 4). Although it is not possible to verify this with testing, we estimate that a similar percentage of fermented and hydrolyzed foods

labeled "gluten free" contain more than 20 ppm of gluten.[5] As we show below in the Detailed Analysis, this means that about 4,700 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. 5). This proposed rule, if finalized, would reduce or eliminate that morphological damage by limiting the "gluten-free" label to foods that are manufactured in a way that minimizes their gluten content.

[5] Producers are making products with qualities that cannot be verified by currently available scientifically valid analytical methods. The rate of defects will be at least as high as for similar products that can be verified, because the chances of getting caught are much lower. The alternative is to assume a higher rate of defects. The more 'gluten-free' products there are in the market that actually have high levels of gluten, the greater the benefits and costs of this proposed rule will be. We do not know how much higher the rate is.

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

The baseline for this economic analysis is full compliance with the gluten-free regulation for all foods that are not fermented or hydrolyzed, and the current market situation for foods that are fermented or hydrolyzed. In order not to double count costs or benefits of the final rule, we estimate how the proposed rule, if finalized, would change health status and producer costs from this baseline.[6]

There is a large degree of uncertainty inherent in this estimation. Each number we use in the calculations is uncertain. To reflect this uncertainty, we define most 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 final numbers are rounded to two or three significant figures, for presentation and to avoid false precision. However, intermediate calculation numbers use all decimal places, to avoid rounding errors.

1. Costs of the Proposed Rule

In order to demonstrate that the food is gluten-free before fermentation or hydrolysis, we expect that most manufacturers would test their incoming ingredients or obtain Certificates of

[6] We are not counting any costs or benefits from products that are subject to TTB labeling requirements. This analysis only covers products subject to FDA labeling regulations. We did not count breweries in the businesses covered when calculating costs, and we did not include alcohol in the diet simulations used to calculate benefits. We have not priced the possible confusion from different regulations or requirements.

Analysis from their ingredient suppliers. While testing is not required nor even expected in all circumstances, it is a reliable way to demonstrate that the ingredient is gluten-free, so we will estimate costs for testing. To the extent that some manufacturers rely on other appropriate verification regarding their ingredients, this analysis may overestimate the total cost. Once a manufacturer evaluates its manufacturing process, if it determines that there is the potential for gluten cross-contact, it must document its implementation of measures to prevent gluten cross-contact. For the purpose of this analysis, we are calling the entire process of evaluating the potential for gluten cross-contact, and development and implementation of measures to prevent it "developing written standard operating procedures (SOPs) for preventing gluten cross-contact." Therefore, for the purpose of this analysis, the costs of this proposed rule are represented as those costs necessary to test the ingredients for gluten, evaluate the potential for gluten cross-contact and if necessary develop written SOPs for preventing gluten cross-contact, relabel products that cannot be brought into compliance, and maintain records of these activities for FDA inspection.

Our estimates of the numbers of manufacturers are based on the number of food products that would be covered by the proposed rule. We searched the FoodEssentials database (Ref.12) for foods that are hydrolyzed, fermented, or contain fermented or hydrolyzed ingredients and bear the claim "gluten-free," "no gluten," "free of gluten," or "without gluten" and found about 2500 products that would be affected by the proposed rule. We estimate that this database has at least half of all products that would be covered by the proposed rule[7], so that there would be, at most, 5000 products affected by the proposed rule.

We do not have any data about how many products are produced in each facility, so we assume that each product and its production line would be tested separately and would require a

[7] The FoodEssentials database is a survey of all products sold in supermarkets, except Wal-Mart store brands. It does not contain some specialty products sold by mail order. We compared the FoodEssentials listing of gluten-free products to the complete listing of products certified by the Gluten-Free Certification Organization, and found a small number of 'Certified Gluten-Free' foods not in the FoodEssentials database. We are also aware of several foods with a gluten-free label that are not certified by this organization or sold in supermarkets, so we used the conservative assumption that the database covered half of the products affected. This assumption may overstate the costs of the rule.

separate evaluation and SOP. If multiple products are produced in the same facility and can share testing, evaluation, SOPs, and paperwork, then costs would be less than these estimates.

We do not know how many of these products are already being manufactured using gluten-free ingredients and/or with a process designed to prevent gluten introduction. A survey of food industry practices (Ref. 20) shows that about 45% of all food production facilities have a written allergen control plan, and about 39% require certificates of analysis for ingredients. Given that producers of foods labeled "gluten-free" are marketing to customers who care more about gluten cross-contact, we estimate that about 75% of the 5000 foods with a "gluten-free" labeling claim already have a written plan for preventing the introduction of gluten into the food product that includes the testing of ingredients and also procedures for evaluating and preventing gluten cross-contact. Therefore, we estimate that testing and SOP development costs would be incurred for about 1250 products. Even facilities that already have an allergen control plan would need to make records available to FDA for inspection and copying, so we estimate that these costs would be incurred for about 5000 products.

a. Testing Costs

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

After paying the startup cost, the producer would then use test kits to test the ingredient on a regular basis, and may also send one or two samples a year to an outside lab for testing. This is a recurring annual cost. We estimate that an average of two ingredients per UPC would be tested in this manner. Most foods affected by this proposed rule are those that contain a single hydrolyzed or fermented ingredient, so any testing would have been done by the ingredient supplier before that supplier performed hydrolysis or fermentation. Other products contain several ingredients that would be tested before fermentation or hydrolysis.

It is also possible that producers would instead obtain a Certificate of Analysis from their ingredient supplier showing that the ingredient does not contain gluten. To the extent that a

single supplier can provide tested ingredients to multiple producers, the cost of the proposed rule would be lower than our estimates.

Testing companies charge between $68 and $110 per sample, with a best estimate of about $75 (Refs. 23, 24). The average of these estimates is about $84 ([68+75+110]/3=84.33), and we also estimate that producers would spend about $28 per sample to collect the ingredient and mail it to the lab[8], for a total cost per lab test of $112 (84.33+27.81=112.14).

Producers would test between 2 and 12 samples of each ingredient (Ref. 21), for an average of 7 samples and an average testing cost of $785 (112.14*7=784.99). Method extension costs between $1,000 and $10,000, with a most likely cost of $2,500 (Ref. 25), for an average cost of $4,500 ([1+2.5+10]/3=4.5).

This results in an average total one-time cost of $5,285 per ingredient tested (785+4,500=5,285). We use Excel's PMT function to annualize this cost over ten years with a discount rate of 7% and find that the annualized cost is $752 per year per ingredient. If the discount rate was 3%, the annualized cost would be approximately $620 per ingredient.

Test kits cost about $11 each and take 10 minutes to use (Ref. 26). The average wage rate in the food manufacturing industry is $32.75 after adding benefits and overhead (Ref. 27) which means that the total cost of using a test kit is about $16.50 (11+[32.75*10/60]=16.46). We estimate that producers would use test kits between twice a year and once a week, with a best estimate of once a month, per ingredient. This yields an average of about 21 test kits used per year, at an annual cost of $351 per ingredient (16.46*21.33=351.1). In addition to using test kits, companies would send between zero and two samples of each ingredient annually to an outside lab, for an average annual cost of $112. Adding up these two costs yields total recurring costs of $463 per ingredient on average (351+112=463).

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[8] A USPS Medium Flat Rate Box costs $12.35 and will hold most food samples. The cost of the food ingredient sent for testing will be about $10. Ten minutes of labor at $32.75 an hour will be required to mail the sample. 12.35+10+(32.75x10/60)=27.81

Adding the average recurring costs to the average annualized one-time costs yields total annual testing costs of $1,216 per ingredient at a 7% discount rate (752+463=1,216) and $1,083 at a 3% discount rate (620+463=1,083) that can be attributed to this proposed rule.

With the average estimate of 1,250 universal product codes (UPCs) requiring testing, and an average of two ingredient tests per UPC, we estimate the total economic costs of testing that result from this proposed rule to be about $3.0 million at a 7% discount rate (1,216*1,250*2=3,040,000) and $2.7 million at a 3% discount rate (1,083*1,250*2=2,707,500).

Table 2 summarizes the variables and the results of the calculations explained above, using mean values for all variables:

Table 2.—Testing Cost Summary

	Per Ingredient	Total
Startup		
Initial tests	7	
Testing Cost	$ 785	
Method Extension	$ 4500	
Total One-time	$ 5,285	$13,200,000
Annualized		
3% Discount Rate	$ 620	$1,500,000
7% Discount Rate	$ 752	$1,900,000
Recurring		
Number of kits used	21	
Cost of Kits	$ 351	
Number of Lab Tests	1	
Cost of Lab Tests	$ 112	
Total Recurring	$ 463	$1,200,000
Total Annual Cost of Testing: 3%	$ 1,083	$2,700,000
Total Annual Cost of Testing: 7%	$ 1,216	$3,000,000

b. Cost of Development and Implementation of Measures to Prevent Cross-Contact

We have estimates for the time and expense of developing allergen control procedures for small facilities. We use these estimates as the cost of evaluating gluten cross-contact risk and developing gluten control procedures for a single UPC. To the extent that multiple UPCs can be

made in the same controlled facility, these estimates overstate the expected cost of the proposed rule.

Based on our expert elicitation (Ref. 28), we estimate that it would take six to eight hours to develop and implement facility-specific procedures for gluten control. This would require the time of professional staff, at a cost of $103 per hour. We also estimate that companies would spend between $0 and $2,000 on allergen control equipment, for a per-UPC average estimate of $1,720 (7*103+1,000=1,720). This is a one-time cost. We use Excel's PMT function to annualize this cost over ten years with a discount rate of 7% and find that the annualized cost is $245 per year per UPC. If the discount rate was 3%, the annualized cost would be approximately $202 per UPC.

Facilities without pre-existing procedures would require regular training in the proper use of the procedures. We estimate that it would take approximately two hours per year to train an employee in the correct use of the procedures. This would require two hours of manager time and two hours per employee, with five to 15 employees being trained. We also estimate that it would take an additional 0.7 hours of manager time per year to update the procedures. This yields an average annual training cost of $933 per UPC (2.7*102.83+2*10*32.75=932.60).

Adding the average recurring costs to the average annualized one-time costs yields total annual SOP costs of about $1,180 per UPC at a 7% discount rate (245+933=1178) and $1,130 per UPC at a 3% discount rate (202+933=1135) that can be attributed to this proposed rule.

With the average estimate of 1250 UPCs requiring the development and implementation of measures to prevent the introduction of gluten into fermented or hydrolyzed food, we estimate the total economic costs of SOP development and implementation that result from this proposed rule to be about $1.5 million at a 7% discount rate (1,180*1250=1,475,000) and $1.4 million at a 3% discount rate (1,130*1250=1,412,500).

Table 3.—SOP Cost Summary

	Per UPC	Total
Startup		
Hours for Development	7	
Equipment Cost	$ 1000	

Total One-time	$ 1,720	$ 2,150,000
Annualized		
3% Discount Rate	$ 202	$ 250,000
7% Discount Rate	$ 245	$ 310,000
Recurring		
Manager Hours for Updating	0.7	
Manager Hours for Training	2	
Worker Hours for Training	20	
Total Recurring	$ 933	$ 1,200,000
Total Annual Cost of Testing: 3%	$ 1,130	$ 1,400,000
Total Annual Cost of Testing: 7%	$ 1,180	$ 1,500,000

c. Relabeling Costs

Producers may decide that it is not possible or economical to make their product in a way that complies with this proposed rule. They may also discover that the products are still not gluten-free after they start a program aimed at compliance with this proposed rule. In either case, they would then remove the "gluten-free" label from the product.

Before the gluten-free regulation was published, testing of foods with "gluten-free" claims showed that 5% of such foods contain more than 20 ppm of gluten (Refs. 4, 9, 10). Therefore, we estimate, as an upper bound, that 5% of foods covered by this proposed rule would be relabeled.

According to the FoodEssentials database (Ref. 12), 2,514 of 271,872 UPCs had a "gluten-free" claim affected by this proposed rule, so we estimate that 0.9% of all foods have such a GF claim (2,514/271,872=0.9%). Because 5% of foods covered by this proposed rule might have to be relabeled, we estimate that 0.05% of all foods would need to be relabeled (0.9%*5%=0.046%).

We used the 2011 Labeling Cost Model (Ref. 29) to calculate the potential new labeling costs implied by the proposed rule. 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 laws are lower if the required changes can be coordinated with planned label changes. We estimate that firms would have one year to comply with the proposed rule. The 2011 Labeling Cost Model

uses a three to four year timeline for normally scheduled redesign, which means that only some of the labeling changes required by this proposed rule can be coordinated with planned labeling changes.

The costs per UPC 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 $148 per label UPC for branded products, the highest estimated cost for a 12 month compliance period is $13,229 per label UPC for private label products, and the midpoint of average estimated cost, adjusting for inflation, is about $6,900 per UPC.

We entered the value of 0.05% of all foods requiring relabeling into the Labeling Cost Model, and the result was that it calculated relabeling costs for 347 UPCs.

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 would have to change their labels earlier than planned. If 347 labels are affected, the proposed rule would affect 317 unscheduled label changes and 30 scheduled label changes. The midpoint of estimated label cost per UPC for a 12 month compliance period is $7,101 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 proposed rule, adjusted for inflation, is estimated to be approximately $2.4 million. This is a one-time cost. We use Excel's PMT function to annualize this cost over ten years with a discount rate of 7% to estimate that the proposed rule would, if finalized, cost approximately $340,000 per year due to label changes. If the discount rate was 3%, the annualized cost would be approximately $280,000.

d. Paperwork Costs

The proposed rule would require manufacturers to maintain records showing that their food products meet the requirements of the proposed rule. The manufacturers would need to make these records available to FDA for inspection and copying.

We estimate that the manufacturers would satisfy the recordkeeping requirements of this proposed rule by maintaining records of their tests or other appropriate verification procedures, their evaluation of the potential for gluten cross contact, and their standard operation procedures for preventing gluten cross-contact. It is also possible that manufacturers would instead comply with this proposed rule by obtaining Certificates of Analysis or test results from their suppliers instead of conducting the testing themselves. In that case, the suppliers rather than the manufacturers would incur the paperwork burdens related to collecting samples for the tests, and the manufacturers would still incur the paperwork burdens related to maintaining records of the tests, in the form of the Certificates of Analysis or test results themselves. If one supplier provides ingredients for multiple manufacturers, then the paperwork burden would be less than these estimates.

The estimates presented here are averages. We anticipate that the records kept would vary based on the type of ingredients used. Some manufacturers, such as those producing fermented dairy products, would likely maintain fewer records. Other manufacturers, such as those producing foods with fermented or hydrolyzed grains, legumes, or seeds, would likely maintain more extensive records.

The costs of testing are detailed earlier in this analysis. We estimate that, in addition to these costs, the proposed rule would require 30 minutes of work per test to process and file the test results so that they can be made available to FDA. This work would cost $33 per hour, for an additional paperwork cost of $16.50 per test.

The one-time method extension requires an estimated average of seven tests per ingredient, so with two ingredients per product, the associated paperwork cost would be $229 per UPC (7*0.5*33*2=229). This is a one-time cost. We use Excel's PMT function to annualize this cost over ten years with a discount rate of 7% and find that the annualized cost is $33 per year per UPC. If the discount rate was 3%, the annualized cost would be approximately $27 per UPC.

We estimate that the manufacturers would use 21 test kits annually on average, per ingredient so the associated paperwork cost would be $688 per UPC (21*0.5*33*2=688). We estimate that the manufacturers would conduct one outside test annually on average per ingredient, so the associated paperwork cost is $33 per UPC (1*0.5*33*2=33).

The costs of developing and updating SOPs are detailed earlier in this analysis. We estimate that, in addition to these costs, the proposed rule would require one hour of work per UPC to make the updated SOP available to FDA, for a cost of $33 per year.

The total annualized paperwork costs per UPC from testing and SOP development are $786 at a 7% discount rate (33+688+33+33=786) and $780 at a 3% discount rate (27+688+33+33=780).

While we estimate that 3750 manufacturers already have testing programs and written procedures in place for gluten control (5000-1250=3750), it is not clear that these manufacturers are maintaining these test results and written procedures a way that would align with the proposed requirements. Therefore, we estimate that all 5000 UPCs would incur these paperwork costs, for a total cost of $3.9 million per year (786*5000=3,930,000).

Table 4.—Paperwork Cost Summary

	Per UPC	Total
Startup		
Method Extension Records	$229	$1,200,000
Annualized		
3% Discount Rate	$ 27	$140,000
7% Discount Rate	$ 33	$160,000
Recurring		
SOP Update Records	$33	$160,000
Test Kit Records	$688	$3,500,000
Lab test Records	$33	$160,000
Total Recurring	$753	$3,800,000
Total Annual Cost of Paperwork: 3%	$780	$3,900,000
Total Annual Cost of Paperwork: 7%	$786	$3,900,000

2. Benefits of the Proposed Rule

To find the benefits of the proposed rule, we estimate the reduction that the rule will likely cause in the number of people who consume harmful amounts of gluten. We then estimate and monetize the QALY gain that results from this reduced consumption of harmful amounts of gluten. Because there are multiple brands available for almost all categories of "gluten-free" labeled food (Ref. 12) and eliminating gluten cross-contact has no effect on the characteristics of the food, we expect that this reduction in gluten consumption will not lead to any offsetting utility losses for consumers.[9]

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

According to the most recent the National Health and Nutrition Examination Survey (NHANES) survey of the civilian non-institutionalized population of the U.S. (Ref. 6), 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[10]. 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*0.14%=429,800).

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

[9] If avoidance of health harms involves eating less-preferred foods, then the monetized benefits of this proposed rule would equal health benefits net of lost consumer utility. However, with this proposed rule, we do not expect such utility loss because: (1) when a producer makes process changes to prevent cross-contact, there is no change to the sensory aspects of final products, and (2) we assume that, in the cases where products are removed from the market, nearly identical products made under controlled conditions will be available as substitutes. If this assumption is incorrect, the unadjusted benefits estimates presented in this analysis overstate the consumer benefits (health benefits minus utility losses) generated by the proposed rule.

[10] 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.

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. 7).

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*68%=292,400).

This does not include people who choose to remain on a gluten-free diet for reasons other than medically diagnosed celiac disease. There are 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 would also benefit from the proposed 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 proposed rule increase if they are included.

b. Estimating Gluten Consumption Change

To estimate the change in gluten intake likely to be caused by this rule, we used gluten testing results of food labeled "gluten-free" before the gluten-free regulation was published, data on diets from the NHANES survey (Ref. 8), and data on the percentage of GF foods that have fermented or hydrolyzed ingredients to simulate gluten-free diets and the daily gluten intake from those diets before and after this proposed rule. These simulated diets consisted of a random selection from fermented or hydrolyzed GF foods, non-fermented or hydrolyzed GF foods, and inherently gluten-free foods not labeled as "gluten-free" and therefore not covered by these rules,

such as raw agricultural commodities, in random amounts matching the observed distribution of serving sizes[11].

Comments from the Celiac Sprue Association to the gluten-free rulemaking (Ref. 4) included test results for 1,000 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. 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. 9, 10) have reported a slightly larger percentage of foods whose gluten content exceeds 20 ppm, but they were not as comprehensive and did not report data for individual food products.

Because it is not possible to test and quantify the gluten content of fermented and hydrolyzed foods, we assume that the distribution of gluten content in these foods is similar to the distribution of gluten content in tested foods. It is possible that the lack of testing has resulted in a situation where fermented and hydrolyzed foods have a greater chance of containing more than 20 ppm of gluten than foods that can be tested. In this case, the benefits of this proposed rule would be greater than the benefits we calculate.

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 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,

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[11] The code for the diet simulations is available at FDA's economics site, in the section for this proposed rule: http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/
As a sensitivity analysis, we also ran simulations that included other sources such as restaurant food and alcohol, under various assumptions about how much gluten is in these sources. None of these simulations had a significant effect on the proposed rule's projected change in gluten consumption.

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.[12]

We then simulated 100,000 gluten-free diets using the @RISK program (Ref. 11). Each diet consisted of a mix of inherently gluten-free unlabeled foods and foods labeled GF. Foods labeled GF consisted of foods that met the requirements of the gluten-free regulation, 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. The remainder of the diet consisted of inherently gluten-free food. Each diet consisted of 15 random draws of an inherently gluten-free food, or from a food labeled GF, according to that diet's proportion of labeled foods. The amount of each food eaten was drawn from the previously defined gamma distribution.

To determine the fraction of foods labeled "gluten-free" that are fermented or hydrolyzed or have fermented or hydrolyzed ingredients, we searched the FoodEssentials database (Ref. 12), a comprehensive survey of food products sold in nationwide in the U.S., for foods with claims about gluten that would be affected by the proposed 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

[12] 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.

hydrolyzed food, based on the text of 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 (2,514/11,108=0.226). We therefore assumed that 23% of all labeled "gluten-free" foods consumed are fermented or hydrolyzed or contain fermented or hydrolyzed ingredients.

We modeled all products covered by the gluten-free regulation as containing up to 19.9 ppm gluten (Foods were drawn from the distribution of tested foods, with foods above 20 ppm removed, and all foods that tested below the limit of quantification of 5 ppm were assigned a random amount of gluten using a uniform distribution between 0 and 5). We used the same estimate for the gluten content of hydrolyzed or fermented foods after this proposed rule is in effect. We estimated the trace gluten content of inherently gluten-free food to be between 0 and 5 ppm.

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. For the purposes of the economic analysis, we choose a 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. 5). This choice underestimates the true benefits of the proposed 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 proposed rule would also reduce intake at those levels.

In the diet simulation, the rule causes a 1.6 percentage point reduction in the number of people with celiac disease on a gluten-free diet consuming more than 50 mg of gluten. This reduction is caused by removing high-gluten hydrolyzed or fermented food with a "gluten-free" label from the market and replacing it with a substitute food that meets the rule's requirements. We multiply the estimate of the reduced 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 4,700 individuals with celiac disease harmed by fermented or hydrolyzed foods carrying the "gluten free" label that are above 20 ppm gluten (1.6%*292,000= 4,672).[13]

c. QALY Gain From Reduced Gluten Consumption

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 5, 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 5.— EQ-5D 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

[13] Implicit in this approach is the assumption that no consumers with celiac disease would be confused by claims (e.g., "processed to remove gluten") that are permitted for products that don't meet the requirements of this rule and thus might contain more than 20 ppm of gluten. Providing support for this assumption is consumer research (Refs. 4, 31) that shows that people with celiac disease insist on words or symbols that say "gluten-free" and distrust other claims.

	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. 13-15). 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. Given the morphological changes caused by 50 mg of gluten (Ref. 12), we generate a low estimate that 50 mg of gluten causes 5% of the harm a normal diet would cause.

We have an estimate that inadvertent partial compliance with the gluten-free diet causes a QALY loss of 0.09 (Ref. 14). We use this to generate a high estimate that 50 mg of gluten causes 30% (=0.09/0.27) of the harm a normal diet would cause.

We have studies showing that prolonged exposure to amounts of gluten smaller than 50 mg daily causes some individuals with celiac disease to report symptoms that lower their quality of life (Refs. 16, 17), but these studies do not provide EQ-5D scores. 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+30+10]/3=15). This means that, on average, an individual with celiac disease who consumes more than 50 mg of gluten daily suffers a QALY loss of 0.035 (0.23*15%=0.0345).

As described in the previous section, 4700 individuals will no longer be harmed by consuming more than 50 mg of gluten from foods covered by this proposed rule, so they will no longer suffer this QALY loss. Their reduced suffering is the benefit of this rule. We estimate that the rule will generate an annual health gain of approximately 160 QALYs (4,700*0.035=164.5) from the reduced gluten in these diets.

d. Monetized Health Benefits

We use the Value of a Statistical Life Year (VSLY) to convert QALY benefits to dollar benefits. Because a VSLY measures the value of an average year of health, and the QALY score of the average American is 0.87, we divide the VSLY values by 0.87 to find the value of a QALY. We repeat our analysis with three different VSLY values, to reflect the uncertainty in the literature on valuation. This results in QALY values of about $130,000; $260,000; and $390,000 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. 18).

Using the middle value of a VSLY, this proposed rule will result in health benefits valued at approximately $41 million annually (160*$258,000=$41,280,000). Using the low value, the value is approximately $21 million annually (160*$129,000=$20,640,000). Using the high value, the value is approximately $62 million annually (160*$388,000=$62,080,000).

Table 6 summarizes the variables and the results of the calculations explained above, using mean values for all variables:

Table 6.—Health Benefits 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 Reduced to Below 50 mg	1.6%
CD-Diagnosed GF Diets Reduced to Below 50 mg of gluten	4,700
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 Gain Caused by Proposed Rule	160
Cost per QALY	$ 260,000
Total Annual Health Gains	$ 41,000,000

e. Other Potential Benefits

NHANES survey data (Ref. 8) 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. 19), 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 proposed 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%*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 proposed rule (0.62/6=0.103), meaning that the benefits of the proposed rule would be double our estimates.

In addition to eliminating diets with more than 50 mg of gluten per day, the proposed rule would reduce the percentage of diets with levels of gluten that might cause lesser harm. Before the rule, about 1.7% of simulated gluten-free diets have between 20 mg and 50 mg of gluten per day. After the proposed rule is in place, about 0.9% 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, then those health problems would be reduced as a result of the proposed 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 proposed rule would be larger than our estimates.

Untreated celiac disease can cause premature mortality in addition to losses in the quality of life (Ref. 1). We do not have any information on the mortality effects of smaller doses of gluten, but it is possible that prolonged exposure to 50 mg of gluten or more also causes premature mortality. By removing this source of gluten contamination, the proposed rule may benefit individuals with celiac disease by preventing early death, in addition to the benefit from improved quality of life.

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 would also benefit from the proposed rule. Anyone who is on a gluten-free diet for any reason would benefit from the reduction in search costs, if they start using and trusting the GF label as a result of this proposed rule.

3. Total Costs and Benefits

The total annualized cost of the testing, evaluation, SOPs, relabeling, and paperwork is $8.8 million at a 7% discount rate (3+1.5+0.3+3.9=8.8) and $8.3 million at a 3% discount rate (2.7+1.4+0.3+3.9=8.3).

Subtracting the costs from the benefits yields net benefits of about $32 million per year ($41 - $8.8=$32).

4. Analysis of Uncertainty

In Tables 3, 4, 5, and 6 of this document and elsewhere we present the expected effects of the proposed rule as point estimates. While this is a convenient way to summarize the effects of the proposed rule and explain our calculation, the use of point estimates neglects the large degree of uncertainty intrinsic to the underlying analysis. In Table 6 of this document, we present the results of a Monte Carlo simulation of uncertainty for the eventual annual benefits and costs of the proposed 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%*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 the proposed 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 proposed 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 $96, peak $103, and maximum $138, reflecting the sum of testing and handling costs. We drew the number of products requiring new testing from a discrete uniform distribution with minimum 0 and maximum 2500.

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 UPC 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.

We drew the number of products requiring new SOPs from a discrete uniform distribution with minimum zero and maximum 2500. We drew the cost of allergen control equipment from a uniform distribution with minimum $0 and maximum $2000.

The labeling cost model produced low, midpoint, and high estimates. Annualized at a 7% discount rate, these are $0.19 million, $0.34 million, and $0.56 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 QALY. Table 7 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[14]. 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% discount rate for all cost numbers.

Table 7.—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	1.4%	1.6%	1.8%
QALY Loss for Untreated Celiac Disease	0.2	0.227	0.27
Average Severity of 50 mg Compared to Untreated	5%	15%	30%
Cost of Lab Test	$96	$103	$138
Products Requiring New Testing	0	1250	2500
Products Requiring New SOP	0	1250	2500
Allergen Control Equipment Costs	$0	$1000	$2000
Initial Lab Tests	2	7	12
Method Extension Cost	$1,000	$2,500	$10,000
Number of Test Kits Used Annually	2	21	50
Number of Annual Lab Tests	0	1	2
Annualized Relabeling Costs (Millions)	$0.19	$0.34	$0.56
Annual Net Benefits: $130k QALY (Millions)	$-1	$11	$30

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

Annual Net Benefits: $260k QALY (Millions)	$6	$32	$69
Annual Net Benefits: $390k QALY (Millions)	$14	$52	$108

For example, using the average ($260,000) estimate for a QALY, there is a 5% chance that the net benefits of the proposed rule are less than $6 million.

Because many uncertainties could not be measured, Table 7 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 would also be individual variability with respect to QALY loss. There is no research that defines the distribution of gluten sensitivity across the population (Ref. 30), so we are forced to make estimations on averages from small and limited studies.

E. Analysis of Regulatory Alternatives

We have identified four regulatory alternatives:

1. Take no action;

2. The proposed rule;

3. Prohibit the "gluten-free" claim on all fermented and hydrolyzed foods; and

4. Limit the requirements of the rule to a subset of fermented and hydrolyzed foods.

1. Take No Action

The baseline for this regulatory analysis is compliance with the gluten-free regulation for all foods that do not contain fermented or hydrolyzed ingredients. For more information, see the Regulatory Impact Analysis for the gluten-free regulation. We assume that, in the absence of this proposed rule, 5% of all foods that contain fermented or hydrolyzed ingredients would contain

more than 20 ppm of gluten. We believe that this would cause harm to individuals with celiac disease that can be avoided at relatively low cost, as we show above in the Detailed Analysis.

2. The Proposed Rule

The costs and benefits of the actions required by the proposed rule are summarized in the Detailed Analysis section above.

3. Prohibit the "Gluten-Free" Claim on Fermented and Hydrolyzed Foods

Another regulatory alternative is to prohibit the "gluten-free" claim on all fermented and hydrolyzed foods, due to the uncertainty in interpreting the results of current gluten test methods for fermented and hydrolyzed foods on a quantitative basis that equates the test results in terms of intact gluten in order to verify their compliance with the 20 ppm requirement.

This alternative would mean that producers who are making good-faith attempts to produce gluten-free fermented or hydrolyzed foods, or foods that contain such ingredients, would have no way to distinguish these products from ordinary products by using the "gluten-free" claim. This would reduce the incentives of producers to market such products. They would not have the option of demonstrating compliance by documenting appropriate ingredients and processes, and would be forced to bear relabeling costs.

This alternative could reduce the chances that individuals with celiac disease are exposed to potentially harmful gluten fragments from fermented and hydrolyzed foods. (It is possible that such gluten could be introduced during the manufacturing process.)

However, the removal of such products from the "gluten-free" market would reduce the dietary options or increase the search costs of people with celiac disease. This could cause them to reduce compliance with the gluten-free diet and suffer health problems as a result.

We believe that these costs are higher than the additional benefits of this alternative. We believe that using gluten-free ingredients and having documented measures in place to prevent the introduction of gluten into the food during the manufacturing process would provide adequate assurance that the amount of gluten in the final product is less than 20 ppm. We believe

that the harm caused by reduced compliance with a gluten-free diet is much larger than the harm that might occur from any trace amounts of gluten in fermented and hydrolyzed foods.

4. Limit the Requirements of the Rule to a Subset of Fermented and Hydrolyzed Foods

Another regulatory alternative is to make the requirements of this proposed rule apply only to a subset of foods deemed to be at high risk of gluten cross-contact, for example legumes, grains, and seeds. This alternative would have lower costs than the proposed rule, but also lower benefits.

Approximately one-fifth of all fermented or hydrolyzed foods labeled "gluten-free" contain legumes, grains, and seeds[15], and these foods are at a higher risk of gluten cross-contact than vegetables, meats and dairy. We estimate that the total annualized costs of this alternative (if the rule only applied to foods that are or contain hydrolyzed legumes, grains, or seeds) would be about $6.8 million less than the total costs of the proposed rule.

As we show in the Detailed Analysis, exposing an individual with celiac disease to 50 mg or more of gluten daily causes a reduction in quality of life valued at approximately $8,800 ($260,000 per QALY*0.035 QALY loss). This means that if this alternative results in more than 780 individuals with celiac disease being exposed to 50 mg or more gluten daily, the additional social costs would be greater than $6.8 million annually (6,800,000/8,800=773).

We believe that at least 780 individuals with celiac disease are being exposed to more than 50 mg of gluten daily as a result of hydrolyzed or fermented dairy, meats, and vegetables; if this assumption is correct, the net benefits of this alternative would be lower than the net benefits of our proposed rule.

[15] This figure excludes distilled vinegar.

Preliminary 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 proposed rule would be its requirement to change "gluten-free" labels on products that do not comply with the proposed rule, the additional testing that may be required, and the additional steps that may be taken to ensure that gluten is not introduced into foods with "gluten-free" labels. At least some of the affected products are produced by small businesses, and some small businesses may own multiple affected products. We estimate that, if the proposed rule is finalized, 319 UPCs would be relabeled, 1,250 UPCs would require testing and SOP development, and 5000 UPCs would face additional evaluation and paperwork burdens, but we do not know how many of them are owned by small businesses.

As a worst-case scenario, an affected product might incur one-time costs of around $8,300 for relabeling, $11,000 for testing, $1,700 for SOP development, and $980 for paperwork, for a total of $22,000 (8,300+11,000+1,700+980=21,980). However, it is unlikely that a producer would pay both relabeling costs and SOP development costs. If the producer chooses to invest in measures to prevent the introduction of gluten, it would probably not be necessary to relabel.

Exempting small businesses from the proposed rule may lift the burden on some small entities. However, because the potential harm done by fermented or hydrolyzed foods carrying the "gluten free" label that are above 20 ppm gluten is so large, and because exemptions would reduce public trust in the proposed rule and cause consumers to incur search costs, such an exception would potentially significantly reduce the benefits of the proposed rule.

Allowing small businesses more time for compliance may lift the burden on some small entities. However, because the potential annual harm done by fermented or hydrolyzed foods carrying the "gluten free" label that are above 20 ppm gluten is so large, and because exemptions during the transition period would reduce public trust in this proposed rule and cause consumers to incur search costs, allowing more time for compliance for some producers would reduce the benefits of the proposed rule.

For example, if one-fourth of "gluten-free" products were produced by small businesses and exempted from the proposed rule, then 0.4% of simulated diets would contain more than 50 mg of gluten daily, resulting in an estimated annual harm of 40 QALYs or $10 million, compared to the baseline of full enforcement. This estimated loss to individuals with celiac disease is far larger than the estimated costs of these businesses complying with the proposed rule.

Unfunded Mandates

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 $141 million, using the most current (2013) Implicit Price Deflator for the Gross Domestic Product. FDA has determined that this proposed rule is significant under the Unfunded Mandates Reform Act. FDA has carried out the cost-benefit analysis in preceding sections. The other requirements under the Unfunded Mandates Reform Act of 1995 include assessing the rule's effects on:

- Future costs;
- Particular regions, communities, or industrial sectors;
- National productivity;
- Economic growth;
- Full employment;
- Job creation; and
- Exports.

We have determined that this rule will not have a significant impact on any of these variables.

Small Business Regulatory Enforcement Fairness Act

The Small Business Regulatory Enforcement Fairness Act of 1996 (Public Law 104-121) defines a major rule for the purpose of congressional review as having caused or being likely to cause one or more of the following: An annual effect on the economy of $100 million or more; a major increase in costs or prices; significant adverse effects on competition, employment, productivity, or innovation; or significant adverse effects on the ability of United States-based enterprises to compete with foreign-based enterprises in domestic or export markets. In accordance with the Small Business Regulatory Enforcement Fairness Act, the Office of Management and Budget (OMB) has determined that this proposed rule is not a major rule for the purpose of Congressional review.

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