

**A Case Study in Implementing the FDA's Interim Guidance for Qualified  
Health Claims: Consumption of Tomatoes, Tomato Products,  
and/or Lycopene and Risk of Prostate Cancer**

**A Ceres<sup>®</sup> White Paper**



Center for Food, Nutrition, and Agriculture Policy  
University of Maryland-College Park

**Authors:**

**Patricia A. Anderson, MPP**

**Gayle L. Hein**

**Richard A. Forshee, PhD**

**Maureen L. Storey, PhD**

Center for Food, Nutrition, and Agriculture Policy  
University of Maryland—College Park  
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## TABLE OF CONTENTS

<b>Abstract</b> .....	<b>i</b>
<b>Introduction</b> .....	<b>1</b>
<b>Methodology</b> .....	<b>2</b>
<i>Performing Initial Search of Available Scientific Literature Related to Proposed QHC</i> .....	2
<i>Verifying Proposed QHC Meets All Code of Federal Regulation (CFR) Preliminary</i> <i>Requirements</i> .....	3
<i>Convening Workshop of Qualified Professionals to Evaluate and Refine Planned</i> <i>Implementation of FDA Guidance</i> .....	3
<i>Collecting, Reviewing, and Evaluating All Relevant Studies</i> .....	3
<i>Rating All Relevant Studies with Internal Validation Procedures</i> .....	4
<i>Convening Workshop for Qualified Professionals to Review and Comment on Draft</i> <i>QHC Petition and Weight of Scientific Evidence</i> .....	5
<i>Evaluating Potential for Disease Risk Reduction in Target Population</i> .....	6
<b>Results</b> .....	<b>6</b>
<i>Literature Review</i> .....	6
<i>Consumer Research</i> .....	7
<b>Discussion</b> .....	<b>8</b>
<b>Table 1. Summary of Quality Ratings and Results</b> .....	<b>15</b>

**Abstract**

The Center for Food, Nutrition, and Agriculture Policy (CFNAP) at the University of Maryland—College Park developed a method to implement the U.S. Food and Drug Administration’s (FDA’s) interim guidance for Qualified Health Claims (QHC) by examining the relationship between consumption of tomatoes, tomato products, and/or lycopene and risk of prostate cancer. The model included a rigorous, systematic approach designed to identify the relevant scientific literature, provide consistent quality ratings of all peer-reviewed primary reports of data collection, fully document the decision-making process and each analysis for the purpose of replication and review, and summarize the overall strength of the evidence using quantitative and qualitative methods. Procedures for internal and external quality control were built into the model at every stage. The model provides an excellent template for QHC petitions, and the FDA’s response to the petition was informative.

## Introduction

Following passage of the Nutrition Labeling and Education Act of 1990, the U.S. Food and Drug Administration (FDA) established general requirements for health claims concerning the relationship between a nutrient and a disease or health-related condition.<sup>1</sup> These requirements included an FDA review of the scientific evidence supporting a health claim prior to its use on food and dietary supplement labels. The evidence was required to meet the FDA's definition of "Significant Scientific Agreement" (SSA). According to the FDA, this standard is met only when the agency "determines, based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence."<sup>2</sup>

In *Pearson v. Shalala*, the plaintiffs challenged the FDA's decision not to authorize health claims for four specific nutrient-disease relationships. The appeals court ruling required the FDA to clarify the SSA standard and to develop a new approach for the evaluation of health claims.<sup>3</sup> Responding to the ruling, the FDA created the Consumer Health Information for Better Nutrition Initiative task force. On July 10, 2003, the FDA issued the final report of the task force, which included the interim Qualified Health Claim (QHC) approval process.<sup>4</sup> This process was designed to encourage a marketplace in which healthy foods can compete; foster research and understanding about diet and health; and protect consumers from misleading claims. The proposed QHC regulatory framework would communicate to consumers both the health claim and the strength of the scientific evidence supporting the claim on the basis of a systematic review of the quality and quantity of scientific evidence that is currently available.

The 2003 initiative established an evidence-based approach to evaluate potential health claims and developed a system of qualifying language to communicate the relative strength of the scientific evidence. The FDA's interim guidance for QHC only requires that the "weight of the evidence" supports the proposed claim.<sup>5</sup> The claim need not rise to the level of SSA. A QHC must use language that avoids misleading consumers about existing scientific uncertainty. The FDA judges proposed claims based on study design types, quality and quantity of applicable studies, consistency of existing evidence, and relevance to disease risk reduction in the target population.

Prostate cancer is the second-leading cause of cancer-related death for adult males in the United States.<sup>6</sup> Lycopene, one of the most potent antioxidants,<sup>7,8</sup> is commonly found in high concentrations in human prostate tissue, and studies have suggested that lycopene may be associated with a reduced risk of cancer, including prostate cancer.<sup>9</sup> Major dietary sources of lycopene include tomatoes and tomato products.<sup>10</sup>

Researchers have attempted to identify the possible mechanisms involved in the relationship between consumption of tomatoes, tomato products, and/or lycopene and reduced risk of prostate cancer. These potential mechanisms include protection against oxidative damage, enhancement of gap junctional communication, suppression of tumor growth, and stimulation of the anti-inflammatory response.<sup>11,12,13,14</sup> Lycopene may also contribute to the detoxification of xenobiotic metabolites.<sup>15,16,17</sup> These mechanisms

suggest a protective role for tomatoes, tomato products, and/or lycopene with respect to prostate cancer. If so, increased consumption of tomatoes, tomato products, and/or lycopene may prove to be beneficial for a significant number of individuals.

**Prostate cancer is the second-leading cause of cancer-related death for adult males in the United States.**

## **Methodology**

### *Overview*

The FDA issued interim guidance for QHC because the process would likely be refined later. CFNAP, therefore, recognized the iterative nature of the QHC process and set out to implement the guidance in such a way as to set the “gold standard” for QHC petitions. To do this, CFNAP applied a rigorous, science-based approach to develop each element of the QHC petition, which included the following:

1. Performing an initial search of the available scientific literature related to the proposed QHC;
2. Verifying the proposed QHC meets all Code of Federal Regulation (CFR) preliminary requirements;
3. Convening a workshop of qualified professionals to evaluate and refine CFNAP’s plan to implement of the FDA guidance;
4. Collecting, reviewing, and evaluating all relevant studies;
5. Rating all relevant studies with internal validation procedures;
6. Convening a workshop of qualified professionals to review and comment on the draft QHC petition and weight of the scientific evidence;
7. Evaluating the consumer research;
8. Evaluating the potential for disease risk reduction in the target population.

### *Performing Initial Search of Available Scientific Literature Related to Proposed QHC*

The FDA requires that a petition for a QHC include the definition of the nutrient-disease relationship; the collection of all studies relevant to the proposed QHC; a classification of each study based on design type; an evaluation of individual study quality; and an evaluation of the strength of the total body of evidence. A preliminary literature search was performed to evaluate whether sufficient research concerning the relationship between consumption of tomatoes, tomato products, and/or lycopene and risk of prostate cancer existed in the public domain to warrant further investigation. CFNAP determined that sufficient prerequisites had been met to proceed with a comprehensive evaluation of the proposed QHC, such as adequate range in study design type, number of studies available for evaluation, number of studies including large sample sizes, number of studies supporting the proposed QHC, and possible mechanisms explaining the nutrient-disease relationship.

*Verifying Proposed QHC Meets All Code of  
Federal Regulation (CFR) Preliminary Requirements*

According to 21 CFR 101.14(a)(2), “[s]ubstance means a specific food or component of food, regardless of whether the food is in conventional food form or a dietary supplement that includes vitamins, minerals, herbs, or other similar nutritional substances.”<sup>18</sup> Tomatoes and tomato products are foods; lycopene in tomatoes and tomato products is a component of food. Therefore, tomatoes, tomato products, and lycopene in tomatoes and tomato products meet the definition of a substance as defined in 21 CFR 101.14(a). In addition, the proposed QHC meets all 21 CFR 101.14 general health claim requirements, *except* for the SSA standard.

The proposed QHC also satisfies the criteria set forth in 21 CFR 101.14(b). There is some scientific evidence that tomatoes, tomato products, and/or lycopene are associated with reduced risk of prostate cancer among an identified U.S. population subgroup—adult males. Tomatoes, tomato products, and lycopene in tomatoes and tomato products contribute nutritive value in accordance with 21 CFR 101.14(b)(3)(i). Tomatoes, tomato products, and lycopene in tomatoes and tomato products are safe and lawful under the applicable food safety provisions of the Federal Food, Drug, and Cosmetic Act.

Furthermore, there is no evidence that establishes an optimum level of lycopene consumption beyond which no benefit would be expected.<sup>19</sup> Foods containing lycopene, including tomatoes and tomato products, have a very long history of use with no indication of significant adverse effects.<sup>20</sup> Several studies have demonstrated that the consumption of tomatoes, tomato products, and/or lycopene is safe and well-tolerated.<sup>21,22</sup> Promoting greater consumption of tomatoes, tomato products, and lycopene in tomatoes and tomato products is also consistent with dietary recommendations of increased fruit and vegetable consumption.

*Convening Workshop of Qualified Professionals to  
Evaluate and Refine Planned Implementation of FDA Guidance*

After developing an implementation strategy, CFNAP invited qualified professionals to a workshop in order to evaluate the plan to implement FDA’s guidance. The objectives of the workshop were three-fold: 1) review FDA’s interim guidance for QHC, 2) present the evidence-based procedure for evaluating the QHC, and 3) discuss the strengths and weaknesses of the proposed implementation procedure. Recommendations for strengthening the QHC implementation strategy were subsequently incorporated into the evaluation procedure.

*Collecting, Reviewing, and Evaluating All Relevant Studies*

The methodology for identifying all studies relevant to the proposed QHC included developing a set of structured literature searches with the assistance of a librarian at the National Library of Medicine. All studies reported in the English language that examined the association between tomatoes, tomato products and/or lycopene and prostate cancer were considered. Studies were identified in the MEDLINE<sup>®</sup>/PUBMED, Biological Abstracts, Science Citation Index, and Clinicaltrials.gov databases.

The Medical Subject Headings (MeSH) tool was used to identify all appropriate search terms for this analysis. Exact search criteria for all databases included combinations of the words ‘lycopene,’ ‘prostate cancer,’ and ‘tomato.’ The search term combinations were used consistently and repeatedly throughout the literature review process to capture newly-published information.

The scientific literature was screened in order to eliminate any primary reports of data collection that were captured by the literature searches but were irrelevant to the proposed QHC. Other relevant articles—such as literature reviews and meta-analyses—were also identified. Studies suggesting an association between consumption of tomatoes, tomato products, and/or lycopene and an increased risk of prostate cancer were not found.

*Rating All Relevant Studies with Internal Validation Procedures*

According to the interim QHC guidance provided by the FDA, the study design types were defined as follows:<sup>23</sup>

**FDA Classification of Study Type**

- 1) Type 1: Randomized, controlled intervention trials
- 2) Type 2: Prospective observational cohort studies
- 3) Type 3: Nonrandomized intervention trials with concurrent or historical controls and case-control studies
- 4) Type 4: Cross-sectional studies, analyses of secondary disease endpoints in intervention trials, and case series

The study design types were characterized only for primary reports of data collection, i.e. data collected specifically for the reported research project. Type 1 studies are considered the most rigorous and, therefore, are given more consideration than the other categories when determining final rank. Conversely, Type 4 studies are given the least consideration. Since the QHC petition process was developed by the FDA, in part, to “[assist] the public in making wise dietary choices that benefit long-term health,”<sup>24</sup> we included all animal and *in vitro* studies in the Type 4 study category. Articles that synthesized or reflected collections of primary reports were not considered part of the rating system, although they did provide useful background information.

The criteria used to evaluate each study included recommendations explicitly mentioned in the interim guidance for QHC as well as other sources cited by the FDA.<sup>25,26</sup> Two evaluation forms were developed to accommodate the differences between randomized, controlled intervention trials and epidemiological studies. In order to maintain consistency, cross-validation of select articles was performed among the

reviewers. The Principle Investigator provided an additional level of internal validation by ensuring that each study was evaluated with the same criteria.

After all relevant studies were individually evaluated, a summary table was completed that showed the number of studies of each design type and their quality ratings. Additional sections of the summary table also noted each study that either 1) supported the proposed QHC and had statistically significant results; 2) supported the proposed QHC and had no statistically significant results; or 3) showed no effect. We also searched for studies that showed any adverse consequences of the proposed QHC, but no such studies were identified. Any studies that could not be classified according to the designated summary categories were listed as ‘N/A’ (**Table 1**).

The overall ranking of the strength of the evidence supporting the proposed QHC was then developed based on the total number of studies as well as the number of observations within each study, consistency among the studies, and relevance to disease risk reduction in the target population or subgroup.

*Convening Workshop for Qualified Professionals to Review and Comment on Draft QHC Petition and Weight of Scientific Evidence*

After drafting the QHC petition, another group of qualified professionals was convened in order to evaluate the strength of the evidence. Participants were asked to identify any research gaps in the scientific literature and to determine the overall strength of the evidence in support of the proposed QHC. After much debate, a consensus about the strength of the evidence and the language to be used for the proposed QHC was reached. The draft petition was also distributed to additional qualified external reviewers for feedback after suggestions from the workshop were incorporated into the document.

*Evaluating Consumer Research*

In order to obtain information about consumers’ awareness, perception, and judgment regarding the proposed QHC, a sample from the National Family Opinion (NFO) panel was surveyed. This sample consisted of 750 male and female adults who had eaten processed tomato products (i.e. ketchup, pasta sauce) in the past 6 months and was nationally representative of adults in the U.S. The sample also included at least 80 males over the age of 40. The survey was designed to test participants’ knowledge of a relationship, if any, between consumption of tomatoes and tomato products, which contain lycopene, and reduced risk of prostate cancer using the following proposed QHC:

- A. Consumption of processed tomato products like ketchup, pasta sauce, tomato juice, or tomato soup, as part of a healthy diet, may reduce the risk of prostate cancer.
- B. Although evidence is not yet conclusive, studies show that consumption of processed tomato products like ketchup, pasta sauce, tomato juice, or tomato soup, as part of a healthy diet, may reduce the risk of prostate cancer.
- C. Growing scientific evidence would suggest that consumption of processed tomato products like ketchup, pasta sauce, tomato juice, or tomato soup, as part of a healthy diet, may reduce the risk of prostate cancer.

Interviewers also asked if the example claims would motivate them to change or rethink their eating habits and in what ways.

#### *Evaluating Potential for Disease Risk Reduction in Target Population*

Relevance of the QHC for disease risk reduction in the target population was addressed by using the risk assessment framework. We analyzed the impact of reasonable increases in tomato product consumption resulting from the proposed QHC among those at risk for prostate cancer.

In order to predict reasonable increases in tomato product consumption based on individuals' response to the proposed QHC, estimates of current lycopene consumption were calculated for adult males using consumption data from two 24-hour dietary recalls collected by the U.S. Department of Agriculture (USDA) in the Continuing Survey of Food Intakes by Individuals, 1994-96 and 1998<sup>27</sup> and the USDA National Nutrient Database for Standard Reference, SR 16.<sup>28</sup> The consumer research was used to estimate predicted increases in lycopene consumption. Reduction in prostate cancer risk was then calculated and compared to a random draw from a probability distribution. This reduction in prostate cancer risk was extrapolated to the entire population at risk of developing prostate cancer (adult males).

## **Results**

### *Literature Review*

A review of the scientific literature examining the relationship between consumption of tomatoes, tomato products, and/or lycopene and prostate cancer risk did not yield any Type 1 studies. Due to the slowly progressive nature of prostate cancer for the vast majority of the male population, randomized, controlled intervention trials are difficult to perform. Randomized, controlled intervention trials are generally more expensive and time-consuming per participant in relation to other types of studies. Attrition and compliance with strict dietary guidelines are also deterrents to a successful randomized, controlled intervention trial.

No Type 1 studies with prostate cancer as the health endpoint were identified in the literature search.

However, the literature search did identify in three randomized, controlled intervention trials that examined lycopene intake among men who had already been diagnosed with prostate cancer. Although these three studies were relatively well-designed and demonstrated an inverse relationship between lycopene supplementation and prostate cancer progression, they were limited for the evaluation of the proposed QHC in that they did not study the relationship between lycopene consumption and prostate cancer prevention.

The literature searches yielded five Type 2 studies, three of which consisted of cohorts of U.S. citizens. The remaining two Type 2 studies examined cohorts from the Netherlands. All five studies had the benefit of containing more than 10,000 participants.

All the Type 2 studies were relatively well-designed and executed. The three studies consisting of cohorts of U.S. citizens showed significant results supporting the proposed QHC. The two studies based on cohorts from the Netherlands did not report a statistically significant relationship and therefore did not provide support for the proposed QHC. Due to the long-term, prospective nature of Type 2 studies, this category provided the strongest overall support of the proposed QHC.

**Type 2 studies provided the strongest overall support for the proposed qualified health claim.**

The Type 3 studies included both case-control studies (n=21) and non-randomized intervention trials with either concurrent or historical controls (n=2). The quality of the studies in this design category varied, as did the overall level of support for the proposed QHC. Eight studies supported the proposed QHC with significant results, although three studies only showed significant results for aggressive cases of prostate cancer. Three studies tended to support the proposed QHC, but the results were not significant. Eleven studies found no statistically significant association and therefore did not support the QHC, and one study was excluded from the evaluation due to conflicting results within the study itself.

The Type 4 studies included one analysis of a secondary disease endpoint in an intervention trial, three animal studies, four *in vitro* studies, and one risk analysis. Even though the interim guidance for QHC issued by the FDA deems Type 4 studies to be less informative for the evaluation of a proposed QHC than the other study types, these studies are still scientifically important. More so than the other types of studies, Type 4 studies tend to look at the mechanisms behind an observed relationship. Eight of these studies supported the proposed QHC and contained significant results. One study supported the proposed QHC but did not achieve significance, while another study was excluded from the evaluation due to conflicting results within the study itself. A complete copy of the QHC petition can be obtained [here](#).<sup>1</sup>

#### *Consumer Research*

Consumer research was conducted to provide information about consumers' awareness, perception, and judgment regarding QHC. The survey found that 45% of adults were aware of lycopene. Among those who were aware of lycopene, 60% believed that it was found in tomatoes and tomato products. Others believed that lycopene was found in vegetables (10%) and/or fruits (11%), while 25% did not know which foods contained lycopene. Also among those aware of lycopene, Claim A received significantly fewer positive comments (74%) than did Claim B (83%) and Claim C (84%). Furthermore, Claim A received a significantly higher number of negative comments than did Claim B. This was the result of respondents perceiving that the general statement in Claim A was not true and/or that processed foods could not be healthy.

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<sup>1</sup> The full Universal Resource Locator (URL) for the QHC petition is:  
<http://www.fda.gov/ohrms/dockets/dockets/04q0201/04q-0201-qhc0002-04-Section-B-02-vol1.pdf>

Regardless of the claim, the majority of respondents agreed that they would “incorporate more tomato products into diet” as a result of the QHC. Most consumers also recognized that lycopene is a natural component of tomato products and correctly answered that “lycopene is not an additive.” For all three claims, the majority of respondents believed that they would need to eat tomato products either 1-2 times/day or 1-2 times/week in order to realize a reduction in prostate cancer risk. Most consumers seemed to properly interpret the potential health benefit of increasing consumption of lycopene and/or tomatoes based on the proposed QHC. Among a set of statements about the relationship between lycopene consumption and prostate cancer, the statement that lycopene “[w]ill reduce the risk of prostate cancer” was selected most often and only 1% of respondents felt that lycopene will “[c]ure prostate cancer.” Consumer research indicates that there is a growing awareness of lycopene and its possible health benefits among the U.S. population and that the majority of consumers were not misled by the tested QHC.

Consumer research indicates that there is a growing awareness of lycopene and its possible health benefits among the U.S. population.

#### *Simulation of Disease Risk Reduction*

This simulation showed a slight reduction in risk of prostate cancer for those individuals in quintiles 1 through 4 of tomato product consumption compared to those at baseline consumption. The simulation also demonstrated a reduction in the number of new reported cases of prostate cancer if consumption of tomato products increased. If this estimated reduction in prostate cancer cases is extrapolated to the approximately 100 million adult men in the U.S. population, this dietary change could potentially reduce the number of new prostate cancer cases by approximately 10,000.

Increasing tomato product consumption by 1 cup per week could potentially reduce the number of new prostate cancer cases by 10,000 per year.

#### **Discussion**

After evaluation of the entire body of evidence, the publicly available data support a QHC that includes “consumption of tomatoes and tomato products, which contain lycopene, may reduce the risk of prostate cancer.” Qualifying language should be added: “although there is scientific evidence supporting the claim, the evidence is not conclusive.”<sup>29</sup> The evidence corresponds most closely to the criteria that the FDA established for a Second Level or ‘B’ claim, as shown below:

- 1) A Second Level or ‘B’ claim is defined by the FDA as a moderate/good level of comfort among qualified scientists that the claimed relationship is scientifically valid. The Second Level is “promising,” but not definitive. High to moderate quality studies of study design Types 1 and 2 and sufficient numbers of individuals must be tested to result in a moderate

degree of confidence that results could be extrapolated to the target population. Additionally, studies of similar or different design would generally result in similar findings and the benefit would reasonably be considered to be physiologically meaningful and achievable under intake and use conditions that are appropriate for such conventional human food and dietary supplements that would be the subject of the claim.

- 2) Plausible mechanisms of action have been proposed and demonstrated in *in vitro* and animal models. The validity of the prospective observational studies is increased because there is theoretical and empirical evidence to explain the observed relationship found in the epidemiological data.
- 3) Increased consumption of tomato products is relevant for reduction of prostate cancer risk among adult males. The evidence suggests that reasonable increases in tomato product consumption could lead to a modest, but meaningful, reduction in the disease burden from prostate cancer. There is no reason to believe that any harm could result from the proposed QHC. Tomato products are Generally Recognized As Safe (GRAS), and there is no evidence of toxicity at any reasonable level of consumption.
- 4) The proposed QHC is consistent with the recommendation in the 2005 Dietary Guidelines for Americans to consume 2 cups of fruit and 2.5 cups of vegetables per day for a reference 2,000-calorie diet. Consumer research showed that consumers would not be misled by the proposed QHC. The research demonstrated that consumers would understand the proposed QHC and respond by increasing their consumption of tomato products.

CFNAP did not find sufficient evidence to support a QHC for a relationship between lycopene supplementation and reduced risk of prostate cancer. The synergistic effects of lycopene with other phytonutrients in tomatoes and tomato products may enhance lycopene's benefits, as demonstrated by other research.<sup>30</sup> One animal study demonstrated that lycopene given in "pure" form did not inhibit chemically-induced prostate cancer in rats, whereas consumption of tomato powder containing an equivalent amount of lycopene showed a positive effect.<sup>31</sup> These results suggest that lycopene in isolation may not confer the same level of protective benefits as lycopene consumed within foods.

In November 2005, the FDA issued its response to the petition and concluded that "there is no credible evidence to support a qualified health claim for tomato lycopene; tomatoes and tomato products, which contain lycopene; lycopene in tomatoes and tomato products; lycopene in fruits and vegetables, including tomatoes and tomato products, and lycopene as a food ingredient, a component of food, or as a dietary supplement and reduced risk of prostate cancer."<sup>32</sup> According to the FDA, there was insufficient evidence to suggest that lycopene by itself reduces risk of prostate cancer. The FDA concurred that "there is very limited credible evidence for qualified health claims for tomatoes and/or tomato sauce, and prostate cancer provided that the qualified claim is appropriately worded so as to not mislead consumers." The FDA put forward the following QHC: "Very limited and preliminary scientific research suggests that eating

one-half to one cup of tomatoes and/or tomato sauce a week may reduce the risk of prostate cancer. FDA concludes that there is little scientific evidence supporting this claim."

Although a total of five intervention studies (three randomized, controlled intervention trials and two non-randomized intervention trials with either concurrent or historical controls) were included in the QHC petition, the FDA could not draw any scientific conclusions from these studies since tomatoes, tomato products and/or lycopene were used as a treatment for men already diagnosed with prostate cancer. One of the criteria by which the FDA evaluates a proposed claim is its potential for disease risk reduction in the target population. The FDA determined that it was scientifically inappropriate to extrapolate the results obtained from studies using individuals already diagnosed with prostate cancer to individuals who did not have the disease. In order to do so, "the available scientific evidence must demonstrate that: (1) the mechanism(s) for the mitigation or treatment effects measured in the diseased populations are the same as the mechanism(s) for risk reduction effects in non-diseased populations; and (2) the substance affects these mechanisms in the same way in both diseased people and healthy people."<sup>33</sup> The FDA determined that such evidence was not available.

The FDA would not draw any conclusions from the review articles, meta-analyses, or abstracts because they did not contain sufficient information on the individual studies that they reviewed. Furthermore, the FDA stated that it "did not consider the animal or *in vitro* studies submitted with the petition as providing any supportive information about the substance-disease relationship because such studies cannot mimic the normal human physiology that may be involved in the risk reduction of any type of cancer, nor can the studies mimic the human body's response to the consumption of tomato lycopene; tomatoes and tomato products, which contain lycopene; lycopene in tomato and tomato products or lycopene in fruits and vegetables, including tomatoes and tomato products. Therefore, FDA did not draw any scientific conclusions from the animal or *in vitro* studies regarding tomato lycopene; tomatoes and tomato products, which contain lycopene; lycopene in tomato and tomato products or lycopene in fruits and vegetables, including tomatoes and tomato products and the reduction of risk of prostate cancer."<sup>34</sup>

The FDA's response to the QHC petition suggests that the agency will require very compelling evidence for 'B' level claims. It is possible that the FDA is setting very high standards for QHC because of the inherent difficulty of communicating scientific uncertainty to consumers. Several consumer-based research studies to assess the effectiveness of various ways of communicating the level of scientific support for health claims on food labels have been conducted by the FDA.<sup>35</sup> The results of these studies suggest that it is very difficult to provide health claims that enable consumers to differentiate between varying levels of scientific uncertainty. We believe these findings underscore the need for a vigorous research program to improve risk communication about the potential risks and benefits of consuming certain foods.

The FDA's position on the types of studies taken into consideration, the strength of evidence required, and its general position with respect to QHC will continue to

evolve. According to the FDA, “scientific information is subject to change, as are consumer consumption patterns. FDA intends to evaluate new information that becomes available to determine whether it necessitates a change in this decision. For example, scientific evidence may become available that will support significant scientific agreement, that will support a qualified health claim for those claims that were denied, that will no longer support the use of the above qualified health claim, or that may raise safety concerns about the substance that is the subject of the claim.”<sup>36</sup> Given the communication challenges, it seems that the FDA will move cautiously with respect to proposed QHC.

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**Table 1.** Summary of Quality Ratings and Results

Design Type	Quality				Total	Results				Total
	+	+/ $\emptyset$	$\emptyset$	N/A <sup>a</sup>		SS	SN	N	N/A <sup>a</sup>	
1										
2										
3										
4										
Total										

<sup>a</sup>The following studies could not be classified according to the designated summary categories (SS, SN, N):

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