Presenting Quantitative Efficacy and Risk Information in Direct-to-Consumer Promotional Labeling and Advertisements

Guidance for Industry

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
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October 2018
Advertising

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Presenting Quantitative Efficacy and Risk Information in Direct-to-Consumer Promotional Labeling and Advertisements Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This draft guidance provides recommendations for presenting quantitative efficacy and risk information in direct-to-consumer (DTC) promotional labeling and advertisements for prescription human drugs and biological products and prescription animal drugs and in DTC promotional labeling for over-the-counter animal drugs[2] (collectively *promotional materials*).[3] For the purposes of this guidance, quantitative efficacy and risk information refers to information that numerically addresses the likelihood or magnitude of a drug's effectiveness or risks.

The guidance outlines FDA's recommendations for how firms[4] that include quantitative efficacy or risk information in DTC promotional materials for their drugs can make the language and presentation more consumer-friendly.[5] These recommendations apply to DTC promotional

[1] This guidance has been prepared by the Office of Prescription Drug Promotion in the Center for Drug Evaluation and Research, in consultation with the Center for Biologics Evaluation and Research and the Center for Veterinary Medicine at the Food and Drug Administration.

[2] The term *drugs* in this guidance refers to prescription human and animal drugs, prescription biologics, and over-the-counter animal drugs.

[3] *Promotional labeling* is generally any labeling other than the FDA-required labeling. Examples of materials that may be considered promotional labeling, such as brochures, booklets, and mailing pieces, are described in 21 CFR 202.1(l)(2). The Federal Food, Drug, and Cosmetic Act (FD&C Act) does not define what constitutes an *advertisement*, but FDA regulations provide several examples, including "advertisements in published journals, magazines, other periodicals, and newspapers, and advertisements broadcast through media such as radio, television, and telephone communication systems" (21 CFR 202.1(l)(1)).

[4] The term *firms* in this guidance refers to manufacturers, packers, and distributors of prescription drugs, as described in this guidance, and over-the-counter animal drugs, including their representatives.

[5] This guidance is not intended to describe whether or when a presentation of quantitative efficacy or risk information would be truthful or non-misleading. FDA reminds firms that they are responsible for ensuring that their promotional materials are truthful and non-misleading and that they comply with applicable statutory and regulatory requirements. See, e.g., 21 U.S.C. 352(a), 352(n), and 321(n); 21 CFR 1.21; and 202.1(e)(5)(i) through (iii). Additionally, we note that there may be ways other than the recommendations provided in this draft guidance that would make presentations of quantitative efficacy or risk information consumer-friendly.

materials regardless of the medium in which they are presented (e.g., print, electronic, audiovisual, broadcast).

This guidance covers the following topics for presenting quantitative efficacy and risk information in DTC promotional materials:

- Presenting probability information in terms of absolute frequencies, percentages, and relative frequencies
- Formatting quantitative efficacy or risk information
- Using visual aids to illustrate quantitative efficacy or risk information
- Providing quantitative efficacy or risk information for the treatment group and the control group

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

The Federal Food, Drug, and Cosmetic Act (FD&C Act) and its implementing regulations generally require that promotional labeling and advertisements for drugs, including materials directed toward consumers, be truthful and non-misleading, convey information about a drug's efficacy and its risks in a balanced manner, and reveal material facts about the drug.[6] Firms generally have flexibility with respect to the presentation of efficacy and risk information about their products so long as the presentation is not false or misleading and complies with other applicable statutory and regulatory requirements. When firms develop DTC promotional materials, they should consider how to best convey information about a drug's efficacy and risks so the audience understands it. This includes consideration of whether to provide efficacy and risk information by using words, numbers, or visual aids, or a combination of these elements.

In recent years, FDA has observed an increase in quantitative presentations of efficacy and risk information in DTC promotional materials submitted to the Agency. Recent research on the communication of treatment information suggests that consumers can recall and comprehend efficacy and risk information when it is provided quantitatively (Buchter et al. 2014; O'Donoghue et al. 2014b; Schwartz et al. 2007; Schwartz et al. 2009; Sullivan et al. 2015; Trevena et al. 2013; West et al. 2013; Woloshin et al. 2004). When compared to qualitative descriptions of efficacy and risk information, quantitative information can improve consumers' accuracy in estimating the drug's benefits and risks (Sullivan et al. 2015; West et al. 2013). This is due in part to how consumers differ in their interpretations of qualitative descriptors (e.g., *rare*, *common*, *most*) and how the context in which qualitative terms are presented can affect how consumers understand them (Buchter et al. 2014; Fagerlin et al. 2007; Lipkus 2007;

[6] See, e.g., 21 U.S.C. 352(a), 352(n), and 321(n); 21 CFR 1.21; and 202.1(e)(5)(i) through (iii).

Visschers et al. 2009). Quantitative efficacy or risk information may offer more precision than qualitative information, which consumers can use to form more accurate perceptions about the drug (Lipkus 2007).

Firms should ensure that DTC promotional materials containing quantitative efficacy or risk information are accurate and understandable. FDA understands that firms may experience challenges when determining how to present this kind of quantitative information in DTC promotional materials. For these reasons, FDA is issuing this guidance to provide recommendations for presenting quantitative efficacy and risk information in DTC promotional materials and to encourage firms to follow these recommendations when including such information in their DTC promotional materials.

The examples in this guidance are intended to illustrate recommended approaches to presenting quantitative efficacy and risk information in DTC promotional materials. Each example is meant to address a specific concept described in the guidance; a given example may not illustrate every recommendation outlined. The examples do not encompass every potential promotional scenario or consideration and do not necessarily reflect an evaluation of a complete promotional piece, including whether the piece complies with other applicable requirements. All recommendations discussed in this guidance should be taken into consideration even if not expressly illustrated in an example.

III. RECOMMENDATIONS FOR PRESENTING QUANTITATIVE EFFICACY AND RISK INFORMATION IN DIRECT-TO-CONSUMER PROMOTIONAL LABELING AND ADVERTISEMENTS

A. Probability Presentations

Firms should consider the following recommendations when presenting quantitative probability information about their drug's efficacy and risks.

1. Absolute Frequencies and Percentages

Firms presenting quantitative efficacy or risk probabilities in DTC promotional materials should convey the information in terms of absolute frequencies (e.g., 57 out of 100) or percentages (57%). Research suggests that using these formats to express probabilities when communicating health information can improve consumers' comprehension and ability to recall the information (Lipkus 2007; Zipkin et al. 2014). Additionally, consumers receiving information about a drug's efficacy and risk rates in terms of absolute frequencies or percentages can more easily process and evaluate the information than when the same information is in a format that requires them to perform a calculation to interpret the probabilities (Lipkus 2007; O'Donoghue et al. 2014b; Sullivan et al. 2015).

Example 1: A firm is developing a magazine advertisement and includes a presentation showing that in clinical trials, most patients experienced a response after

12 weeks of treatment with Drug X. The firm wants to add numeric values to the presentation to help consumers understand this information.

To communicate this information in a manner that will facilitate consumer comprehension, the firm presents the information as an absolute frequency: *In a clinical trial, 78 out of 100 patients experienced a response after 12 weeks of treatment with Drug X.*

Example 2: A firm plans to include quantitative information in a patient mailer for Drug X about the most common adverse reaction associated with Drug X: nausea.

To allow consumers to easily process this information, the firm presents the information as a percentage: *In a clinical trial, 45% of patients experienced nausea during 12 weeks of treatment with Drug X, compared to 18% of patients during treatment with Drug Y.*

2. Relative Frequencies

Research suggests that consumers do not understand relative frequencies (e.g., 33% reduction in symptoms; 3 times as likely to experience a side effect) in health communications as easily as they understand other formats for presenting probabilities, such as absolute frequencies or percentages (Covey 2007; Fagerlin et al. 2007; Zipkin et al. 2014). Consumers may also find the efficacy or risk probability described as a relative frequency harder to comprehend and more favorable as compared to the absolute frequency, which could lead to consumers' over- or underestimating how well the drug works or the magnitude of the risk associated with the drug (Ancker et al. 2006; Covey 2007; Zipkin et al. 2014).

If firms choose to present efficacy or risk probabilities as relative frequencies, they should add context to the relative frequency presentation to improve consumers' ability to accurately understand the efficacy or risk information. Specifically, firms should include the corresponding absolute probability measures in presentations of relative frequency measures to provide the information in a way that does not require further calculation about the effect being communicated (Covey 2007; O'Donoghue et al. 2014b; Sullivan et al. 2015).

Example 3: A firm is developing a DTC television advertisement for Drug X, which is indicated to reduce the risk of stroke. In a clinical trial, the following absolute risk reductions were observed: 1% of patients treated with Drug X had a stroke, compared to 2% of patients in the control group. This represents a 50% relative reduction in risk of stroke.

To communicate this information in the DTC television advertisement in a manner that will facilitate consumer comprehension, the firm presents the absolute risk percentages in direct conjunction with the 50% relative risk reduction information: *In a clinical trial, Drug X reduced the risk of stroke by 50% (1% of patients treated with Drug X had a stroke, compared to 2% of patients in the control group).*

B. Formatting Quantitative Efficacy or Risk Information

Firms that provide quantitative efficacy or risk information about their drugs in DTC promotional materials should incorporate the following formatting recommendations:

- Present the information in the same numerical format throughout a promotional labeling piece or advertisement (Lipkus 2007; Trevena et al. 2013). For example, firms providing two probabilities about two efficacy outcomes should provide both probabilities as absolute frequencies or both probabilities as percentages. Firms should also consistently characterize efficacy or risk information quantitatively throughout a promotional piece, rather than alternating between qualitative descriptors and quantitative information to describe similar information or concepts.

- Use frequencies with the same denominator when providing more than one absolute frequency and consider using denominators that are multiples of 10 (Fagerlin et al. 2007; Lipkus 2007; Trevena, et al. 2013; Visschers et al. 2009).

- Express probabilities using whole numbers to the extent that the probabilities in whole numbers accurately reflect the numerical value being described in the promotional piece (Lipkus 2007; Zipkin et al. 2014).[7] Where a whole number would not be appropriate, firms should express the value as is (e.g., as a decimal) instead of rounding the value up or down to the nearest whole number. For example, firms should not round probabilities less than 1 to the nearest whole number. Similarly, firms should not round probabilities to the nearest whole number when comparing probabilities that are so close in value that the difference between the probabilities would be lost if the values were expressed as a whole number or numbers. Firms also should ensure that quantitative probability information about a particular risk does not minimize or deter from information about the severity of the risk. For example, firms should not disproportionately emphasize the low probability of a serious risk occurring as a way to detract from the seriousness of that risk.

Example 4: A firm is developing a consumer brochure for Drug X and is considering whether to describe quantitative information about moderate symptom relief in patients treated with Drug X and treated with placebo in terms of absolute frequencies (9 out of 10 and 3 out of 10, respectively) or as percentages (90% and 30%, respectively).

Although either probability measure would be appropriate to describe these outcomes, to help consumers process the information, the firm should provide the outcomes for both the treatment and placebo groups in the same format (i.e., both outcomes as absolute frequencies or both outcomes as percentages): *In patients*

[7] For values greater than 1, to express a value to the nearest whole number, the following principles apply: For amounts falling exactly halfway between two whole numbers or higher (e.g., 2.5 to 2.99), round up (e.g., 3); for values less than halfway between two whole numbers (e.g., 2.01 to 2.49), round down (e.g., 2).

treated with Drug X, 9 out of 10 patients experienced moderate symptom relief, compared to 3 out of 10 patients who received placebo. Alternatively: *In patients treated with Drug X, 90% of patients experienced moderate symptom relief, compared to 30% of patients who received placebo.*

Example 5: In a clinical trial for Drug X, 54% of patients treated with Drug X experienced moderate symptom relief and 19% of patients treated with Drug X experienced complete symptom relief, compared to 28% of patients treated with placebo and 2% of patients treated with placebo, respectively. The firm is developing a patient booklet for Drug X that contains the following information: In a clinical trial, the majority of patients experienced moderate symptom relief after treatment with Drug X, and 19% of patients experienced complete symptom relief. In patients treated with placebo, less than half of patients experienced moderate symptom relief and 2% of patients experienced complete symptom relief.

To present the information consistently, the firm should include the "*majority of patients (54%)*" and "*less than half of patients (28%)*" in the proposed patient booklet. Alternatively, the firm could consistently present only the quantitative information throughout the piece (e.g., *"…54% of patients treated with Drug X experienced moderate symptom relief...," "...28% of patients treated with placebo experienced moderate symptom relief..."*).

C. Visual Aids

When DTC promotional materials contain quantitative efficacy or risk information, visual aids such as graphs, tables, and icon arrays can be used to illustrate the information and put the numerical values in context. Visual representations of efficacy and risk in DTC promotional materials improve consumer comprehension of numeric values by illustrating patterns, summarizing the data, and reducing the amount of mental calculations the consumer must perform to extract meaning from the quantitative information (Ancker et al. 2006; Fagerlin et al. 2007; Lipkus 2007). Moreover, visual aids can improve consumers' ability to accurately understand how well a drug works and support decision making (Fagerlin et al. 2007; Garcia-Retamero and Cokely 2013; Sullivan et al. 2016; Zipkin et al. 2014).

Visual aids in DTC promotional materials help consumers comprehend quantitative efficacy and risk information, but all visual aid designs are not equally effective in conveying all types of information (Fagerlin et al. 2007; Sullivan et al. 2016). Therefore, we recommend that firms select the visual aid design that best communicates the quantitative efficacy or risk information being presented. When choosing a visual aid to express quantitative efficacy or risk information about a drug, firms should carefully consider the communication's purpose and objectives (Ancker et al. 2006; Fagerlin et al. 2007). For example, a bar graph is an appropriate format for visually depicting comparisons between probabilities, whereas a line graph is more useful for illustrating trends or changes over time (Ancker et al. 2006; Fagerlin et al. 2007; Lipkus 2007). Additionally, firms should consider the following general recommendations when designing visual aids to illustrate quantitative efficacy or risk information in their DTC promotional materials:

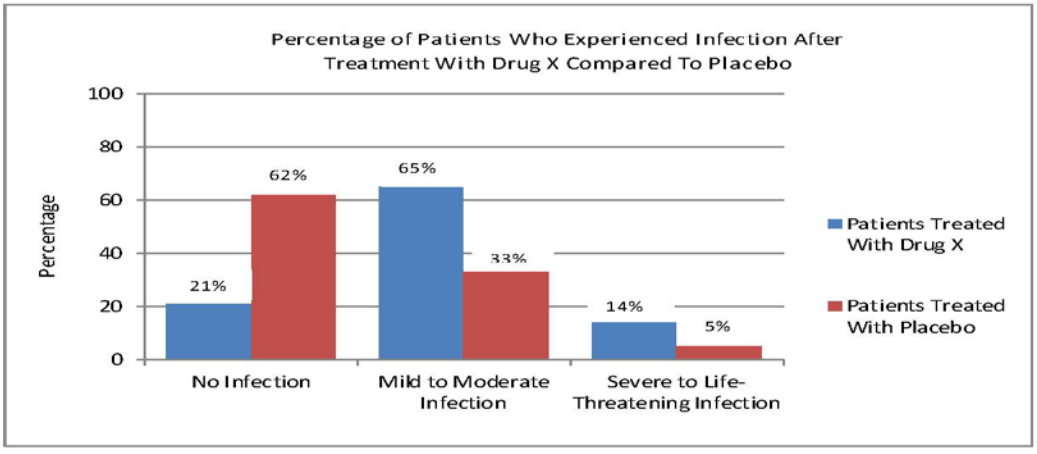
- Explain the purpose of the visual aid clearly and accurately and define the elements displayed (Garcia-Retamero and Cokely 2013; Lipkus 2007). For example, firms should include a title, header, or caption (written or oral depending on the media) and identify the visual aid's variables, scales, and axes (when applicable).

- Make visual displays of numeric information proportionate to the quantity being described (Ancker et al. 2006; Lipkus 2007). For example, the height of a bar on a bar graph should be proportionate to the quantity it represents.

- Include visual representations of both the numerator and denominator of ratios or frequencies (Ancker et al. 2006). For example, an icon array should illustrate the number of people who experienced the effect (numerator) out of the total number of people studied (denominator).

Example 6: Infection is a risk associated with the use of Drug X. The firm responsible for Drug X wants to include a visual aid on Drug X's consumer website to communicate information from Drug X's approved labeling about the number of patients who did not experience an infection, those who experienced a mild to moderate infection, and those who experienced a severe or life-threatening infection after treatment with Drug X compared to patients treated with placebo.

The firm prepares a bar graph to present this information because it best facilitates the comprehension of visual comparisons between probabilities. As illustrated below, the firm includes a title that describes what the bar graph portrays, labels the scales and variables, and ensures that the values graphically displayed are proportionate to the quantities being described.



D. Quantitative Efficacy or Risk Information from the Control Group

Firms that provide quantitative efficacy or risk information about a drug in DTC promotional materials should provide quantitative information from both the treatment group and the relevant control group. Information from the control group plays an important role in evaluating a drug's

benefits and risks (O'Donoghue et al. 2014a). Including efficacy or risk measures observed in the control group quantitatively when providing corresponding quantitative measures observed in the treatment group improves consumers' ability to process and comprehend the drug's efficacy and risks and can lead to more-informed decision making (O'Donoghue et al. 2014a; Schwartz et al. 2009). Research suggests that consumers can use the information about the control group to form accurate perceptions about a drug's efficacy and risk (O'Donoghue et al. 2014a; Schwartz et al. 2009; Sullivan et al. 2013). When including control group information in promotional materials, firms should also ensure that they accurately describe the comparator used in the control group.

Example 7: In a clinical trial of 173 participants, 68% of patients who were treated with Drug X plus a sulfonylurea experienced a reduction in blood glucose levels, while 33% of patients treated with a sulfonylurea alone experienced a reduction in blood glucose levels. The firm is developing a social media web page for Drug X and includes a presentation that 68% of patients treated with Drug X plus a sulfonylurea experienced a reduction in blood glucose levels.

The firm should also include that 33% of patients treated with a sulfonylurea alone experienced a reduction in blood glucose levels.

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