



**sanofi aventis**

Because health matters

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Date 10-April-2007

Via fax and UPS

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

**Re: Docket No. 2007D-0040**

*Draft Guidance for Industry on Developing Products for Weight Management*

Dear Sir/Madam:

Sanofi-aventis U.S. Inc, a member of the sanofi-aventis Group, appreciates the opportunity to comment on the above-referenced Draft Guidance entitled "**Developing Products for Weight Management**".

**GENERAL COMMENTS**

- Obesity is a disease in its own right and the FDA should recognize it as such in line with the Directive of the Secretary of Health and Human Services released in July of 2004. The document should therefore be renamed "Draft Guidance for Industry on Developing Products for the **Treatment of Obesity**"
- The requirement and expectation of the agency for **weight maintenance** are not sufficiently explained in terms of outcomes and duration.
- There is no information on the evaluation of **weight regain** (rebound) after treatment cessation and methodology for its evaluation. This is, however an important efficacy and safety parameter.
- Prevention of **weight gain associated with smoking cessation** is lacking. This is an important health issue and this guidance should be the opportunity to include provisions similarly to what is provided for drug-induced weight gain.
- Section on **Combinations** is not complete and not in line with other guidelines on Combos.
- We acknowledge that the need for a **run-in period** has been removed.

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**SPECIFIC COMMENTS:**

**Lines 22-25:** *This guidance applies to products intended to be used for **medical weight loss**, which can be defined as a long-term reduction in fat mass with a goal of reduced morbidity and mortality through quantifiable improvements in biomarkers such as blood pressure, lipids, and HbA1c.*

This guidance addresses three issues: (a) weight management, (b) medical weight loss, and (c) obesity.

“Weight management” is a broad category including prevention of weight gain in both overweight and obese patients and in the non-overweight category as well as weight gain in populations experiencing involuntary weight loss, such as patients with HIV/AIDs, some cancers and other wasting diseases. Therefore, it is too broad for the content of the guidance.

“Medical Weight Loss” is also a broad category encompassing which begs the question, “*What is non-medical weight loss?*” We also observe that other guidances issued by the FDA address disease states.

Since the document is really about treating obesity (as defined by Body Mass Index cut points) we suggest that the document be re-named, “*Draft Guidance for Industry on Developing Products for the **Treatment of Obesity***”

**Lines 22-25:** *This guidance applies to products intended to be used for medical weight loss, which can be defined as a long-term reduction in fat mass with a goal of reduced morbidity and mortality through quantifiable improvements in biomarkers such as **blood pressure, lipids, and HbA1c**.*

Are these merely biomarkers? Should these be considered clinical endpoints or at least surrogate endpoints since changes in blood pressure, lipids, and HbA1c are already accepted as valid indications?

Further, there are numerous comorbid conditions associated with obesity in addition to the above listed cardiometabolic factors.

A putative obesity drug product, which reduced excess adipose tissue even without reduction in these cardiometabolic parameters, would be a useful product. The excess mass would be likely to reduce strain on the musculoskeletal system, which would be an important health objective, by reducing disability. Reduction in fat mass alone would probably cause a reduction in stigmatization, which is a well-recognized aspect of obesity.

A precedent for such approval has occurred when the Food and Drug Administration approved human growth hormone for the treatment of small stature in children. To the best of our understanding, short stature is not associated with excess mortality and morbidity. However, the teasing, bullying and social isolation of children with short stature was deemed sufficient to allow a product to address this problem.

It is fundamentally unfair to hold one physiological condition, obesity, to a different standard than another physiological condition, small stature.

**Lines 29-33:** *The September 1996 draft guidance is being revised to provide advice on conducting studies to evaluate the efficacy and safety of products for weight management in patients with medication-induced weight gain and weight management in obese pediatric patients. Recommendations on the design of studies evaluating the efficacy and safety of combinations of weight-management products are also provided.*

It is unclear whether this document is still restricted to “patients with medication-induced weight gain”, “obese pediatric patients”, or “combinations of weight-management products”, as mentioned in these lines.

**Lines 36-38:** *...however, weight loss and weight maintenance should be demonstrated over the course of at least 1 year before a product can be considered effective for weight management.*

Weight loss should be demonstrated over the course of one year and weight maintenance should be demonstrated over the course of a second year (two-years total) before a product can be considered effective for weight management.

Two adequate and well-controlled trials should be considered in the demonstration of weight management.

**Lines 41-42:** *This guidance also does not discuss the general issues of clinical trial design or statistical analysis.*

Modification suggested:

“This guidance discusses the specific issues related to weight management, but not the general issues of clinical trial design or statistical analysis.”

**Line 72:** *Obesity is a chronic, relapsing health risk defined by excess body fat.*

Obesity is properly understood as a **disease** in its own right. A standard definition of “disease” requires two of the following three indicia: (a) specific causes or causes (etiology), (b) a collection of signs and symptoms, and (c) consistent anatomical alterations. (Stedman’s Medical Dictionary, 25<sup>th</sup> Ed.) Obesity clearly meets all three indicia.

The presence of a disease can occur with or without subjective feelings of being unwell or social recognition of that state. A person with undetected high blood pressure or diabetes might feel to be in good health but would properly be considered to have a disease.

Obesity meets all reasonable definitions of “disease” and is recognized as a disease in the International Classification of Diseases published by the World Health Organization in ICD-9, (Code 278.0) and in ICD-10 (Code E66). Obesity has been recognized as a disease by sister federal agencies including the Social Security Administration (65 Fed. Reg. 31039), the Internal Revenue Service (IRS Revenue Ruling 2002-19) On July 15, 2004, Health and Human Services Secretary Tommy Thompson announced that the Centers for Medicare and Medicaid Services would remove language “obesity itself cannot be considered an illness” in the Medicare coverage manual, removing a significant barrier to coverage of anti-obesity treatments.

**We recommend that the first sentence of Line 72 be replaced by the following language:**

*“Obesity is a long term, chronic, fatal and relapsing disease in which the principal sign is excess adipose tissue. Obesity is a phenotypic disease that has primary etiologies (e.g. “primary obesity”, hypogonadotropic hypogonadism, Prader-Willi syndrome), secondary etiologies (e.g. Cushing’s disease, hypothyroidism) and may even be drug induced. The etiology of “primary obesity” is multifactorial. Increased adiposity is caused by genetic, environmental, behavioral and hormonal factors. It has been established that there are neuroendocrine factors that affect body mass, appetite, and satiety. Excess adiposity alone causes a number of changes in the body’s lipids metabolism. Obesity significantly affects the musculoskeletal and cardiovascular systems. Obesity is well established as the cause of many important health conditions (referred to as comorbid conditions) including type 2 diabetes, heart disease, hypertension, stroke, dyslipidemia, metabolic syndrome, sleep apnea, osteoarthritis of the knee and hip and some cancers. Obesity is strongly associated with numerous, other adverse health conditions, including but not limited to, depression, reproductive disorders including birth defects, reduced quality of life and psychosocial problems. Preventing weight gain and reducing excess adipose tissue accumulation are significant public health goals. To achieve one or both goals, single drugs or drugs in combination may act on one or more mechanisms that promote excess adiposity. These may include reduction of hunger/appetite, enhancement of satiety, alteration in food preferences, enhancement of physical activity, increases in energy expenditure or enhancement of fat oxidation. In addition to the known mechanisms of increased adiposity, a drug may be targeted at novel mechanisms or strategies that are, at this time, unknown.”*

**Line 84:** ... increase in a *curvilinear* or linear manner with BMIs...

“linear” is clear, while “curvilinear” means any sort of curve.  
Why not “in a linear or **non linear** manner”?

**Lines 91-92:** *Table 1. Weight Classification Guidelines.*

Please clarify whether this classification is applicable to any type of adult population or some adjustments should be made for non-Caucasian populations such as Asian populations.

**Lines 144-146:** *The American Academy of Pediatrics (AAP) defines a pediatric-aged patient with an age- and sex-matched BMI of greater than or equal to 95th percentile as overweight or obese.*

In children, a BMI between 85th and 95th percentile for age and sex is considered at risk of overweight, and BMI at or above the 95th percentile is considered overweight or obese (Himes JH, Dietz WH., Guidelines for overweight in adolescent preventive services: recommendations from an expert committee. Am J Clin Nutr. 1994;59:307–316; US Dept Health and Human Services. The Surgeon General’s Call to Action to Prevent and Decrease Overweight and Obesity. Rockville, D: US Department of Health and Human Services, Public Health Service, Office of the Surgeon General; 2001).

**Lines 148-153:** *For patients aged 2 to 7 years, the AAP recommends weight loss through lifestyle modification if the BMI is greater than or equal to the 95th percentile for age and sex with the presence of one or more comorbidities. For patients who are 7 years of age or older, weight loss through lifestyle modification is recommended if the BMI is between the 85th and 95th percentile for age and sex with the presence of one or more comorbidities or if the BMI is greater than or equal to the 95th percentile for age and sex regardless of the presence of comorbidities.*

In the light of the increasing epidemic of overweight in children, the committee on Nutrition of the AAP (Pediatrics, 2003, 112; 424-430) recommends routine assessments of eating and activity patterns in children and BMI assessment throughout childhood. If there is an excessive weight gain, address this with parents and other caregivers, even before children are severely overweight.

The statement is: it is likely that anticipatory guidance about diet, weight and physical activity, or treatment intervention before obesity has become severe will be more successful.

**Lines 178-179:** *Studies should be designed to differentiate the efficacy of all the active doses versus placebo.*

This is not clear.

A study designed as a dose response with a trend test should be sufficient.

**Lines 199-202:** *The lifestyle modification programs used in the preapproval trials should be applicable to individual patients prescribed the product post-approval (i.e., programs should strike an appropriate balance between effectiveness and simplicity).*

The prerequisite regarding lifestyle modification programs (diet, exercise...) both before (during placebo run in phase) and during study treatment should be more detailed in term of target outcome, duration, etc.

**Lines 209-212:** *Effort should be made to include in the studies a representative sample of patients from the various demographic, ethnic, and racial groups in which the prevalence of obesity is highest. Development programs also should include a representative sample of patients with extreme obesity (BMI greater than 40 kg/m<sup>2</sup>).*

Appropriate representation of obese Type 2 diabetic patients should be considered.  
Also, give reference (and examples) for populations with high prevalence of obesity.

**Lines 216-226:** *The number of subjects necessary to demonstrate the efficacy of a weight-management product will be smaller than the number needed to adequately assess safety. A reasonable estimation of the safety of a weight-management product upon which to base approval generally can be made when a total of approximately 3,000 subjects are randomized to active doses of the product and no fewer than 1,500 subjects are randomized to placebo for 1 year of treatment.*

*For example, the above sample size will provide 80 percent power to rule out with 95 percent confidence an approximately 50 percent increase in the incidence of an adverse event that occurs at a rate of 3 percent in the placebo group (i.e., 4.5 percent versus 3 percent). This sample size also should allow for efficacy and safety analyses to be conducted within important subgroups such as sex, ethnicity, and baseline BMI*

No rationale is provided to support why the required safety database for a drug to treat obesity should be substantially larger than that required for drugs to treat other chronic conditions. This would only be appropriate if the potential benefit was unusually low, or if anti-obesity treatments were inherently less safe than most other drugs. Weight loss of 5-10kg has been shown to substantially reduce the risk of developing diabetes, improve back and joint pain, and reduce sleep apnea.

The size of safety database is also dependent on the pharmacology and experience with compounds of the same class.

**Lines 230-239:** *The efficacy of a weight-management product should be assessed by analyses of both mean and categorical changes in body weight.*

- *Mean: The difference in mean percent loss of baseline body weight in the active-product versus placebo-treated group.*
- *Categorical: The proportion of subjects who lose at least 5 percent of baseline body weight in the active-product versus placebo-treated group.*

For co-primary endpoints, please clarify if they should be achieved both or only one (use of "AND" or "OR"). Page 7, lines 276-285, seems to indicate that it is "OR" (i.e., it only requires either of the two endpoints being achieved).

**Lines 235-236:** *Mean: The difference in mean percent loss of baseline body weight in the active-product versus placebo-treated group.*

Please clarify whether absolute change from baseline in body weight can be used as the primary endpoint, instead of percent loss of baseline body weight.

Page 5, lines 187-188, seems to indicate that either absolute change or percent change in body weight can be chosen as the primary endpoint. Therefore, we suggest revision for line 235: from "percent loss" to "absolute or percent loss" for consistency, unless justifications against this revision can be provided. **Subsequently:**

- Page 7, lines 276-280, it would be helpful to provide efficacy benchmark for absolute change in body weight.
- Page 12, lines 491-492, please revise: from "change from baseline" to "absolute or percent change from baseline".
- Page 12, line 513, please revise: from "(percentage)" to "(absolute or percentage)".

**Lines 241-250:** *Secondary efficacy endpoints should include, but are not limited to, changes in the following metabolic parameters:*

- *Blood pressure and pulse*
- *Lipoprotein lipids*
- *Fasting glucose and insulin*
- *HbA1c (in type 2 diabetics)*
- *Waist circumference*

As secondary endpoint, the percentage of patients losing at least 10% of baseline body weight in the active-product versus placebo-treated group is also of interest.

**Lines 254-258:** *Because the evaluation of investigational weight-management products routinely includes assessment of changes in patients' metabolic profiles, and in some cases may involve measurement of visceral fat content by CT or MRI, waist circumference should not serve as a surrogate for visceral fat content when measured in a clinical trial investigating the efficacy of a product for weight loss.*

Considering references on page 3, lines 93-102 [which states that: "***Waist circumference, like BMI, is inexpensive and easy to measure and correlates with CT- and MRI-derived measurements of visceral fat content (Pi-Sunyer 2004)***"], and easy measurements of waist circumference, how can it be justified that waist circumference "*can not serve as a surrogate for visceral fat content*"?

**Lines 263-267:** *Since weight loss is expected to improve these comorbidities, an important secondary efficacy endpoint should be the proportion of subjects treated with the weight-management product compared with placebo who have a meaningful dose-reduction or complete withdrawal of their concomitant medication.*

This paragraph does not reflect the clinical reality of treatment with such concomitant medications. Neither labeling, nor widely accepted practice guidelines for antihypertensive, lipid lowering agents or anti-diabetics provide such specific rules for dose adjustments and discontinuation. Thus, it is not realistic to expect that a sponsor could provide their own guidelines, could enforce such guidelines, or that the data collected would be sensitive to any drug effect.

**Lines 29-33:** *In general, a product can be considered effective for weight management if after 1 year of treatment either of the following occurs:*

- *The difference in mean weight loss between the active-product and placebo-treated groups is at least 5 percent and the difference is statistically significant*
- *The proportion of subjects who lose greater than or equal to 5 percent of baseline body weight in the active-product group is at least 35 percent, is approximately double the proportion in the placebo-treated group, and the difference between groups is statistically significant*

This is in contradiction with the (co-) primary endpoint in line 232, which states that: *“The efficacy of a weight-management product should be assessed by analyses of both mean and categorical changes in body weight.”*

**Lines 279-280:** *The difference in mean weight loss between the active-product and placebo-treated groups is at least 5 percent and the difference is statistically significant.*

Should an “observed” be added before the first occurrence of the word “difference”?  
Or should the null hypothesis be interpreted as:

$$H_0 : \mu_1 < \mu_0 + 5\%$$

where  $\mu_1$  is the mean percent reduction from baseline for treatment and  $\mu_0$  is the mean percent reduction from baseline for placebo?

**Lines 282-285:** *The proportion of subjects who lose greater than or equal to 5 percent of baseline body weight in the active-product group is at least 35 percent, is approximately double the proportion in the placebo-treated group, and the difference between groups is statistically significant.*

Similarly, should the “proportion of subjects” be the “observed proportion of subjects”?  
In addition, guidelines for other drug classes generally do not specify a minimum magnitude of effect. If such a requirement is to be made the specific magnitudes of effect must be justified on the basis of risk-benefit. (From a regulatory point of view, if there was no risk how can a drug be non-approvable if there is benefit to some patients?)

**Lines 289-290:** *Therefore, changes in common weight-related comorbidities should be factored into the efficacy assessment of investigational weight-management products.*

How should this be interpreted? Are comorbidities to be included as regressors in linear or logistic regressions in the primary analysis? The statement is unclear.

**Line 308:** *In general, patients should have baseline HbA1c levels between 8 percent and 10 percent.*

This HbA1c range is rather high, as we try to target patients with HbA1c less than 6%. Furthermore, more patients with diabetes are now aggressively treated to below 8%. Please consider changing “between 8 percent and 10 percent” to “between 7 percent and 10 percent”.

**Lines 321-323:** *To ensure that drug or biologic-induced weight loss is caused primarily by a reduction in fat content, not lean-body mass, a representative sample of study subjects should have a baseline and follow-up measurement of body composition by DEXA, or a suitable alternative.*

As the FDA has pointed out, should consider waist circumference as a valid indicator that weight loss is caused primarily by reduction in fat.

**Lines 341-342:** *For centrally acting weight-management products, sponsors should anticipate the need to conduct preclinical and clinical studies of abuse liability.*

Clearer guidance and input needed from the Controlled Substance Staff regarding the abuse liability assessment of centrally-acting drugs.

**Lines 360-362:** *We recommend that the efficacy and safety of fixed-dose combinations be compared with the individual product components of the combination and placebo in phase 2 trials of sufficient duration to capture the maximal or near-maximal weight-management effects of the products.*

Unfortunately, there is nothing in this section about combinations (including fixed-dose combinations) of a weight loss drug with another drug like antidiabetics. The importance of this type of FDC should be developed.

This request for conducting a dose-ranging is not consistent with the guidance “*Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products*”, which states that:

*“For a drug known to be effective as monotherapy, a single adequate and well-controlled study is usually sufficient to support effectiveness of the drug when combined with other therapy (as part of a multidrug regimen or in a fixed-dose combination).”*

**Lines 29-33:** *However, a fixed-dose combination that is associated with **at least twice** the weight loss observed with that of each of the individual components will be viewed more favorably than combinations that do not achieve this degree of relative weight loss.*

Why putting the objective of a FDC so high?

When an effective weight loss drug is combined with a second drug, may be not so effective alone, the additional weight loss is always interesting especially when associated with effect on other risk factors (glucose, lipids, etc). Therefore, even a smaller weight loss could be of interest. And again other type of combinations are possible not only targeting weight.

**Lines 370-371:** *Once a fixed-dose combination has been deemed more effective than its individual components, the combination can then be examined versus placebo in phase 3 trials.*

After a fixed-dose combination has been demonstrated to be more effective than its individual components, what is the primary objective of the Phase 3 trial for comparing the combination versus placebo: for safety assessment? Please be more specific.

Again, this is not in line with the guidance “*Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products*”. In addition, it is not clear here if we can avoid inclusion of individual component arms in late-stage Phase 3 when superiority over component has been established in Phase 2 dose ranging trial.

**Lines 381-382:** *A number of drugs, notably psychotropic and some anticonvulsant agents, are associated with moderate-to-marked weight gain*

This section should not focus on CNS drugs only, but should be more general.

**Lines 394-396:** *Patients eligible for participation in trials examining the efficacy and safety of products for the treatment of medication-induced weight gain should have a documented increase in body weight of at least 5 percent within 6 months of starting a drug known to cause weight gain.*

This is one valid approach.

However, another approach should be recognized: for drugs with known weight gain, it is desirable to start that drug and the weight-loss medication at the same time so as to prevent such weight gain (in patients already at high BMI, e.g., >27).

**Lines 420-423:** *Because of issues related to safety and possibly efficacy that are unique to the particular combinations of drugs studied, approval of a product for weight management in patients with medication-induced weight gain generally will be limited to the weight-inducing drug studied and will not apply to the drug class in which the compound is a member.*

We think that a balance should be reached between limiting the Indication to the weight-inducing drug studied (as proposed) and the drug class indication. For practical reasons it seems difficult to perform as many studies as compounds available if the number of compounds is high (> 10 for example). On the other hand if the efficacy is evidenced on 3 different drugs of the same class perhaps a class labeling could be acceptable. Results of CT should also be used for extrapolation?

**Lines 439-441:** *Pharmacokinetics and dose-ranging studies generally should include patients with age- and sex-matched BMIs greater than or equal to the 95th percentile.*

**Lines 445-447:** *Eligible patients should have age- and sex-matched BMIs greater than or equal to the 95th percentile (see <http://www.cdc.gov/growthcharts>).*

If studies in children are done, age and sex adjusted BMI percentiles should be used. In global studies, mostly the IOTF percentiles (international standards: Cole et al, BMJ 2000; 320, 1240) which give international cut off points for BMI for overweight and obesity by sex between 2 and 18 years, defined to pass through body mass index of 25 and 30kg/m<sup>2</sup> in adults, would be adequate if the studies are performed worldwide as the percentiles differ considerably in between different ethnicities (even within the US - Hispanics!) and countries.

**Lines 444-445:** *We suggest that initial pediatric studies be limited to adolescents (i.e., 12 to 16 year olds).*

Adolescents go up to 18 years not only 16. Otherwise, specify: "at inclusion".

**Lines 447-449:** *Patients should have a documented history of failing to lose sufficient weight with lifestyle modification before enrollment into studies of a weight-management product.*

As there is no common lifestyle modification program existing for children worldwide (not even a common one in the US!): what is considered adequate to document history of failing? And what should be continued throughout the trial?

**Lines 461-464:** *Because linear growth should be taken into account when assessing changes in the body weight of children and adolescents, the primary efficacy parameter in weight-management trials of pediatric patients should be a function of the change in BMI (e.g., the mean percent change in BMI and the proportion of patients who lose greater than or equal to 5 percent of baseline BMI).*

Please clarify whether absolute change in BMI can be used as the primary endpoint for the “mean” analysis.

**Lines 489-494:** *The number of subjects in a placebo-controlled trial should be the maximum of sample sizes calculated based on the co-primary endpoints of categorical response defined as greater than or equal to 5 percent reduction in baseline body weight after 1 year, and change from baseline weight. Calculations should be based on two-sided tests of significance at the 5 percent level and at least 80 percent power. Effect sizes for the calculations should represent clinically meaningful differences.*

Same as p 6, i.e., clarify co-primary endpoints with “AND” or “OR”.  
Also, if both co-primary endpoints must be achieved, a statement mentioning that the risk of overpower, in case more patients are included for better safety evaluation (see section Trial Size Duration, p 6), is compensated by the categorical criteria that, if achieved, imply clinical significance.  
In addition, please specify what are the clinically meaningful differences. Page 7, lines 279-285 seem to provide the clinically meaningful differences for percent and categorical changes in body weight, but what about the absolute change in body weight?

**Lines 498-504:** *Historically, there have been high rates of premature subject withdrawal in long-term trials of weight-management products. To allow for a true intent-to-treat (ITT) analysis, we encourage sponsors to obtain body weight measurements in all subjects who prematurely withdraw from late-stage preapproval trials near the calendar date at which they were scheduled to complete the trial (Simons-Morton and Obarzanek et al. 2006). For example, a subject who withdraws from a 12-month study after 6 months of treatment should have a body weight measurement at the time he or she would have completed 12 months of study participation.*

Clarify whether the evaluations performed after study withdrawal are to be used in the primary mITT population or for sensitivity analysis. Current practice is to ignore post-treatment data in the primary efficacy analysis.

**Lines 525-527:** *If statistical significance is achieved on the co-primary endpoints, type 1 error should be controlled across all clinically relevant secondary efficacy endpoints intended for product labeling.*

If possible, please articulate how to control type 1 error for secondary efficacy endpoints when only one of the two co-primary efficacy endpoints is significant based on a multiplicity adjustment (e.g., Hochberg procedure).

**Lines 560-563:** *Thus, for a weight-management product to obtain a stand-alone indication for the prevention or treatment of type 2 diabetes, dyslipidemia, hypertension, or any other weight-related comorbidity, it should be shown that the product effectively prevents or treats the comorbidity through a mechanism that is independent of weight loss.*

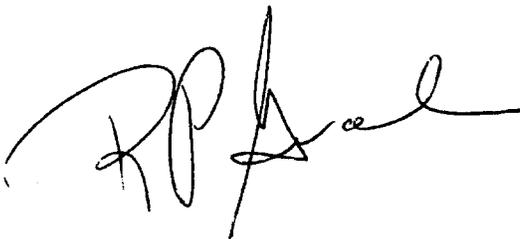
We acknowledge the requirement for demonstration of a weight-independent effect. Nevertheless, in evaluating the additional claims, it is the total effect that should be considered. From a patient and a healthcare provider point of view, it is the total magnitude of the effect that is important, not just the weight-independent part.

**Lines 577-580:** *Ideally, a therapeutic product intended to treat metabolic syndrome should normalize or improve all components of the syndrome, independent of weight loss (see section VIII), and ultimately be shown to prevent the development of type 2 diabetes and reduce cardiovascular morbidity and mortality.*

Such description is purely theoretical. Rather than “*Ideally*”, the agency should describe what could be acceptable for gaining the Metabolic Syndrome indication.

Sanofi-aventis appreciated the opportunity to comment on the Draft Guidance entitled “Developing Products for Weight Management” and are much obliged for your consideration.

Sincerely,



Richard P. Gural, Ph.D.  
Vice President  
Regulatory Development