Individuals of low-literacy and non-Caucasian ethnicity were underrepresented in the study population.

- There is a lack of objective and prospective data collection (subject weights, dietary compliance, use of a multivitamin, adverse event recording)

- Reimbursement procedures during the study and certain questions during the telephone interview may have influenced subject behavior during the study.

- The three month actual use study duration is shorter than the six month proposed duration of use and does not assess subject continuation/ discontinuation of use behaviors after either three or six months or orlistat use. We do know that 16% of orlistat users discontinued orlistat use due to adverse events during the three month study period and that 46% of orlistat purchasers (of the 148 reached for telephone interview) were still using orlistat on Study Day 90.

This actual use study was not designed with weight loss efficacy endpoints, but the data collected suggest that most subjects lost weight while using orlistat 60 – 120 mg TID in the OTC setting. The mean measured weight loss at the end of study participation was 3.3 kg based on objectively measured weights at the pharmacy in 106 of 237 (44.7%) users who returned to the pharmacy for a last visit as requested. Based on measured weights taken at study day 60 and beyond, 42% of subjects lost more than 5% of their body weight; however, this figure is based on weights from only 25% of the user population. Based on self-report at the final telephone interview, 41% of all study subjects using orlistat lost more than 5% of their body weight, and the mean weight loss was 4.8 kg. However, self-reported weight loss data is based only on reported weight loss for orlistat users who actually lost weight. Data on individuals who did not lose weight or gained weight during the study were not included in these calculations. For comparison, obese and overweight subjects (BMI = 28 – 43 kg/m^2) who enrolled in randomized, placebo-controlled studies and used orlistat 60 mg and 120 mg lost an average of 4.26 kg and 4.65 kg respectively with six months of treatment; however, weight loss above and beyond that of the placebo group averaged 2.4 – 2.8 kg. Weights during the randomized, controlled trials were objectively measured by study personnel. In general, individuals with higher BMIs lost more weight than those with lower baseline BMIs both in controlled clinical trials and in the actual use study. The percent body weight lost is fairly consistent across the range of BMIs.

From a safety perspective, the primary concerns with OTC orlistat use are:

- the potential for fat-soluble vitamin deficiencies, especially with continuous or intermittent chronic use

- the potential for cyclosporine users with organ transplants to use the product and increase their risk of organ rejection.

During the actual use study, the percentage of orlistat users who used a multivitamin correctly increased from 38% at the 14-day follow-up telephone interview to 53% at the 90-day follow-up

telephone interview. The increase in MVI compliance may have resulted from the educational effects of the CATI interview process. Despite the increase in correct MVI use with orlistat, a minimum of 47% of subjects using orlistat were not using a MVI correctly. The label used for the AUS placed MVI use instructions under *Other information* in the Drug Facts label. Consistent with the label submitted to the NDA, the MVI use instructions in the LC study label were in the *Directions* section of Drug Facts (see Appendices 10.4 and 10.5). Comprehension of this label element was 73%. Label comprehension and differences in label directions for MVI use on orlistat and MVI containers may influence compliance with correct MVI use. Additional changes in label language addressing correct MVI use may increase consumer comprehension and compliance.

The eligible study population included two cyclosporine users. Although the label stated, *Do Not Use if you are taking cyclosporine (a drug given after transplant surgery),* one of the two cyclosporine users self-selected into the study. Post-marketing adverse event reporting includes a few cases of acute graft rejection in individuals using cyclosporine and orlistat. Orlistat decreases cyclosporine absorption and concomitant use may result in subtherapeutic levels. Labeling language that explicitly mentions the risk of organ transplant rejection may improve compliance with this label warning. Immediately after the advisory committee meeting, FDA received a self-selection study on cyclosporine users. This study, along with a warfarin self-selection study submitted concurrently, will be reviewed separately due to the timing of the submission. These studies may offer additional information about self-selection and label comprehension in these potential consumer groups.

Overall, almost half of eligible subjects self-selected correctly into the study, but 54% selected incorrectly. Among eligible study subjects with labeled exclusions, 77% made an incorrect self-selection decision. Some of this data is driven by the fact that 74% of eligible subjects met the label exclusion *more than 30 pounds to lose*, which is not a labeled exclusion on the NDA label. Study subjects with conditional or unconditional labeled exclusions made correct self-selection/de-selection decisions 0 – 50% of the time depending on the particular labeled exclusion. In the actual use study, it is not clear whether the low correct decision rates reflect deficiencies in label comprehension or whether subjects understood the label and made their decisions based on other factors. Results of the label comprehension study (see the review by Susanna Weiss, Ph.D.) suggest that label elements regarding unconditional and conditional exclusions were generally well understood with comprehension levels > 85%. This reviewer again notes that the label used in the label comprehension study (which was conducted after the AUS) was identical to the label submitted to the NDA except that it did not include the *Do Not Use if you are not overweight warning*.

All weight loss agents raise the concern of misuse or abuse by consumers who are not overweight or have an eating disorder such as anorexia, bulimia, or binge-eating. Among female subjects in the actual use study, 8.9% of the orlistat users were not overweight by BMI criteria, but many of these women perceived themselves to be overweight. This reviewer recognizes reasonable situations where an individual with a *normal* BMI would choose to use orlistat for a limited period of time to lose a few pounds while remaining within the normal BMI range. Such individuals may feel better or improve other health conditions, like joint pain, at a slightly lower

but normal weight. Given the safety profile of orlistat, this may be an appropriate OTC use for this drug. Unfortunately, consumers with eating disorders sometimes misuse OTC drugs such as weight loss agents and laxatives. Orlistat exerts a physiological effect only when fat is present in the diet. Among individuals with anorexia nervosa who practice severe dietary restriction and eat little fat, orlistat would be unlikely to effect weight loss. While 50% of individuals with anorexia nervosa do exhibit some binging and purging behavior, the binges are usually small.[1] This reviewer was unable to find any published reports of individuals with anorexia nervosa using orlistat. Individuals with bulimia often induce vomiting or use cathartics following a binge.[1] In these individuals, orlistat would probably inhibit the absorption of about one third of the consumed fat in the diet, and the remainder of dietary nutrients would be absorbed normally. Based on weight loss realized by study subjects using orlistat and dose ranging studies (by Roche, Inc.) that demonstrated near maximum inhibition of fat absorption at the 120 mg dose, bulemics would be unlikely to achieve the immediate or substantial weight loss with orlistat use that they seek and sometimes achieve with other purging methods. A literature search revealed four published case reports of bulimic women who used orlistat with each binging episode to inhibit fat absorption and weight gain.[2, 3, 8] Two of these women used orlistat as their only purging mechanism.[3] Binge-eaters comprise about two to four percent of the obese population, and 75% of binge-eaters are obese.[1] Two published studies suggests that orlistat is effective for weight loss in individuals diagnosed with binge eating disorder when combined with behavioral therapy.[4, 6] The primary safety concern in the small portion of consumers with eating disorders may be the same as that for all OTC orlistat users: the risk of fat soluble vitamin deficiencies developing over time with chronic use.

As mentioned previously, a preliminary review by Cynthia Kornegay, Ph.D. in ODS suggests a possible association between orlistat use and pancreatitis when using sibutramine as a crude comparator as well as the AERS database as a whole. Prescription labeling for orlistat does include a warning about cholelithiasis. A more detailed ODS review is underway.

9.2 Recommendation on Regulatory Action

This reviewer believes that this application is **approvable** when the entirety of data regarding orlistat safety and efficacy and label comprehension are considered together with the actual use study results. Nearly all orlistat users dosed orlistat according to label directions and followed a diet plan, and 92% of orlistat users were overweight or obese by strict BMI criteria. Despite poor self-selection results in the actual use study, the label comprehension study, performed with a label nearly identical to the proposed NDA 21-887 label, suggests that label warnings were understood by more than 85% of consumers

An approvable action with correction of identifiable deficiencies (see Section 9.5) is recommended.

An addendum to this review will be added when the ODS report on the potential association between orlistat use and pancreatitis is completed and reviewed.

9.3 Recommendation on Postmarketing Actions

None at this time.

9.4 Labeling Review

Please see the review by Arlene Solbeck, M.S. from the Division of Nonprescription Regulatory Development.

9.5 Comments to Applicant

Consistent with recommendations from the January 23, 2006, Advisory Committee meeting, stronger, more explicit language is needed in the *Do Not Use* warning for cyclosporine users and the *Ask before use* warning for warfarin. More effective labeling language is needed to describe correct multivitamin use while using orlistat OTC. In addition, the *Do Not Use if you are not overweight* label element should be tested. Following the label modifications, the final proposed label should be tested in a label comprehension study that incorporates a self-selection process.

10 APPENDICES

10.1 Scripted CATI telephone interview questions

Scripted questions for follow-up interviews included the following:

- Have you started to use the orlistat yet?
- Do you plan to use the medicine?
- When do you intend to start using the medicine? (A callback was set for this date and the subject was told that a follow-up call would be make to see if they started the medicine)
- Since you were in the pharmacy to enroll in this study, have you spoken with a health care professional? What did you talk to this health care professional about? (Nurse describes what subject and health care professional spoke about). Whom did you speak with (No specific contact information was obtained).
- Since you were in the pharmacy to enroll in this study, have you referred to the information on the label for any reason?
- When you read the label at the pharmacy, were there things you didn't understand or had questions about?
- What things on the label didn't you understand or did you have questions about?
- There were some support materials that came with the orlistat. Have you read or used any of that material since you first got the medicine at the pharmacy?
- There was a web site mentioned on the box the medicine came in. Did you visit the web site?
- On the days you used the medicine,
  - On average, how many capsules did you use per day?
  - How many times a day did you take the orlistat?
  - Typically how many capsules did you take each time?
- Were there times you took fewer capsules? Why did you take fewer capsules on those occasions?
- Were there times when you took more capsules at a time? Why did you take more capsules on those occasions?
- Since you started to use the medicine, have there been periods of time in which you didn't use the medicine? Why did you choose not to use the medicine? How long, on average, were the periods of time in which you did not take the medicine?
- Since enrolling in the study, approximately what percent of days would you say you used the medicine?
- When did you usually take the medicine? You indicated that there were times when you did not take the medicine with meals. Can you tell me why?
- How often do you take the multivitamin? How do you take it in relation to the orlistat? Did you start taking the vitamin before or after you started taking orlistat?
- Do you exercise? Since you enrolled in the study, how many times per week do you exercise? Is this more, about the same, or less than before you enrolled in this study?

About how long do you exercise each time? Is this more, about the same, or less than before you enrolled in the study?

- Are you following any kind of diet? Is this a supervised diet? Who supervises your diet? What kind of diet are you on?
- How successful are you maintaining this diet?
- Since you enrolled in this study, have you had any discomfort or changes in your health status? What was the discomfort or change?
- Since enrolling in the study, have you gone to the hospital for any reason? What was the reason for your hospital visit? Were you admitted as an inpatient? What was the date that you went to the hospital? What was the date that you were released from the hospital?
- Since you first started to use the orlistat, have you started any new medicines? This would include medicine your doctor prescribed, medicine you can buy without a prescription, vitamins, or dietary supplements?
- Have you become pregnant since you enrolled in this study? What is your due date?
- Since you started using the study medicine, have you lost any weight? About how many pounds have you lost?
- How satisfied are you with this medicine? Could you please explain why?
- Are you still using the study medicine? What was the last date you used the medicine? Do you plan to use it again? When do you plan on using it again? (Nurse uses judgment to classify answer as will use again within 3 months of enrollment, after more than 3 months since enrollment, or don't know).

End of Study Questions:

- Would you purchase the product again? Why?
- Do you think this product was effective in helping you to lose weight? How?
- Why do you think it was not effective in helping you lose weight?
- When you enrolled in the study, you indicated that you have _____. Did you talk with a doctor about this condition either before or after using the medication?
- Why didn't you consult with your doctor before using the product?
- What did the doctor say when you talked with him?
- Why didn't you talk with your doctor?
- Many detailed questions about type of diet subject is using and how often subject eats certain kinds of foods.
- Many detailed questions about reading nutritional labels, reducing fat in diet, target calories, understanding how to calculate calorie and fat information
- What type of activity best describes the type of exercise you typically do? Why do you exercise?
- Did you use any of the materials included in the orlistat package or the dietary and lifestyle information? Which ones? How useful were they? How much do you use them?
- Did you visit the website? How useful was it?
- Is there anything else you would like to tell me about your use of the medicine or your participation in the study? What else would you like to tell me?

10.2 Defecation Pattern/Adverse Event Worksheet

Defecation Pattern/Adverse Event Worksheet

1. Symptom: _____			Start Date: _____	2. Symptom: _____			Start Date: _____
Inconvenient:	❑ Yes	❑ No	Stop Date: _____	Inconvenient:	❑ Yes	❑ No	Stop Date: _____
Most Inconvenient:	❑ Ongoing:	❑ Duration: _____		Most Inconvenient: ❑	Ongoing: ❑	Duration: _____	
3. Symptom: _____			Start Date: _____	4. Symptom: _____			Start Date: _____
Inconvenient:	❑ Yes	❑ No	Stop Date: _____	Inconvenient:	❑ Yes	❑ No	Stop Date: _____
Most Inconvenient:	❑ Ongoing:	❑ Duration: _____		Most Inconvenient: ❑	Ongoing: ❑	Duration: _____	
5. Symptom: _____			Start Date: _____	6. Symptom: _____			Start Date: _____
Inconvenient:	❑ Yes	❑ No	Stop Date: _____	Inconvenient:	❑ Yes	❑ No	Stop Date: _____
Most Inconvenient:	❑ Ongoing:	❑ Duration: _____		Most Inconvenient: ❑	Ongoing: ❑	Duration: _____	

Events with Different Start/End Dates:

Each event could be an AE and should be considered separately according to the following guidelines:

- Asterisked items are always AEs.
- Non-asterisked items are only AEs if they are inconvenient.

Events with the Same Start/End Date:

For each start/end date there should only be one AE:

- Asterisked events will always be an AE, but 2 or more asterisked events will be combined into 1 AE.
- A non-asterisked event will only be an AE if it is the most inconvenient one.
- If the subject can't decide which event is the most inconvenient, then all events will be combined into 1 AE.

  Exception:

- There may be 2 AEs if there is a combination of asterisked and non-asterisked events and the non-asterisked event is the most inconvenient of them all (the most inconvenient non-asterisked event will be one AE ...g AE.

10.3 Defecation Pattern Terms, Definitions, and Rules

Defecation Pattern Change Term	Definition
*Fecal Incontinence -	Uncontrolled, spontaneous defecation
*Oily Spotting -	Uncontrolled seepage of oil without stool
*Flatus with Discharge -	Flatus with small amounts of stool or oil
*Fecal Urgency -	Urgent, but controlled, need to produce stools
*Oily Evacuation -	Controlled discharge of oil without stool
*Fatty/oily Stool -	Stools mixed with fat or with a separate oily layer
Liquid Stools -	Stools almost all liquid with very few solid parts
Increased Defecation -	Increased frequency of bowel movements
Soft Stools -	Stools mushy and deliquescent (i.e., stools not formed but of rather fluid consistency)
Decreased Defecation -	Decreased frequency of bowel movements
Pellets -	Stools hard and in the shape of small pellets

1. (*) Attributable to the pharmacological action of orlistat and are always considered as adverse events.

When a subject reported an event that fell into one or more of the categories described above, interviewers asked the following questions to help accurately identify and describe the adverse experience.

1. Was the event controlled or uncontrolled?
2. Was it oil alone, stool alone, or oil mixed with stool?
3. Was the discharge of oil or stool with or without flatus?
4. When did the symptoms start and stop?
5. Was it inconvenient?

The following rules for describing adverse changes in defecation patterns were used.

1. Items marked with an asterisk (*) in this dictionary are attributable to the pharmacological action of orlistat and are always considered as adverse events. These items appear in the list in decreasing order of clinical significance.
2. Terms without an asterisk may represent variations in normal defecation patterns and therefore are considered to be adverse events only when described by the patient as inconvenient.
3. Distinct events occurring at different time points should be reported as separate adverse events.
4. Several events occurring at the same time will be reported as followed: The item described by the patient as most inconvenient should be reported as the adverse event;
    A. If the most inconvenient event is not an asterisked item and there is at least one asterisked item occurring at the same time, the most descriptive term will be reported as a separate adverse event. All of the asterisked items and any remaining non-asterisked ones will be reported as a single adverse event;
    B. If no single item can be identified as most inconvenient, then all items should be reported as one single adverse event.
5. Any adverse experience occurring simultaneously but not listed above should be reported as a separate adverse event.

10.4 Drug Facts Label used in Actual Use Study

Drug Facts

Active ingredient (in each capsule)	*Purpose*
Orlistat 60 mg	Weight loss

Use
- to promote weight loss when taken with a reduced calorie diet

Warning(s)

Allergy alert: Do not use if you are allergic to orlistat or any of the ingredients in this product.

Do not use
- if you are taking cyclosporine (a drug given after organ transplant surgery), warfarin (blood thinning medicine) or prescription medicines for diabetes

Ask a doctor before use if you have any of the following conditions
- problems absorbing food (malabsorption)
- gallbladder problems
- more than 30 pounds to lose
- been given a diet recommended by a doctor
- diabetes, high blood pressure, or high cholesterol/triglyceride levels.

Ask a doctor or pharmacist before use if you are
- taking medicines for high blood pressure or high cholesterol/triglyceride levels. These prescription doses may need to be changed during weight loss.
- taking any other weight loss medications or supplements.

When using this product
- do not exceed recommended dose (see Directions).
- some of the fat in the food you eat will not be absorbed into your body.
- you may experience gastrointestinal changes such as diarrhea-like symptoms, fatty stools, gas with discharge, and increased bowel movements, especially after meals containing more than 30% fat. *These changes are a natural effect of this product stopping some of the fat from being absorbed into your body. They are often temporary and generally subside within the first weeks of taking the product.*
- eating meals that are low in fat and calories will help you lose weight and also may reduce these side effects. *Remember, for best results, you should be on a reduced-calorie diet that contains no more than 30% fat.*
- read the enclosed user's guide for more information on these side effects.

Stop use and ask a doctor if
- you have an allergic reaction to this product.
- you do not have noticeable weight loss after 3 months of product use.

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- Before using this product, please read the enclosed user's guide for complete directions and other important information.
- This product is for mild to moderately (up to 30 pounds) overweight adults 18 years and older.
- Take 1 to 2 capsules (60 mg) with each meal containing fat, up to 3 times a day.
- This product can be used for up to 6 months of continuous use. If you would like to continue use beyond 6 months, please read the enclosed user's guide.

Other information
- This product can reduce the level of vitamins in your body. Therefore, you should take a daily multivitamin 2 hours before or 2 hours after taking this product.
- Store at 15 to 25°C (59 to 77°F). Keep bottle tightly closed.

Inactive ingredients:
FD&C Blue No. 1, gelatin, microcrystalline cellulose, povidone, sodium lauryl sulfate, sodium starch glycolate, talc, titanium dioxide

Questions or comments? Call toll free **1-800-XXX-XXX**

10.5 Drug Facts label submitted with NDA 21-887

Drug Facts

Active ingredient (in each sealed capsule) — **Purpose**
Orlistat 60 mg ..... Weight Loss Aid

Use
- promote weight loss in overweight adults when used along with a reduced calorie and low fat diet

Warnings
Do not use
- if you are taking cyclosporine (a drug given after organ transplant)
- if you have been diagnosed with problems absorbing food
- if you are allergic to any of the ingredients in orlistat capsules
- if you are not overweight

Ask a doctor before use if you have
- gallbladder problems or kidney stones

Ask a doctor or pharmacist before use if you are
- taking medicine for diabetes. Your medication dose may need to be adjusted during weight loss.
- taking warfarin (blood thinning medicine)
- taking other weight loss drugs

When using this product
- you should follow a well-balanced diet that is reduced in calories and contains 30% fat or less. Try starting this diet before you begin taking orlistat capsules. See enclosed Companion Guide for information and tips on how to follow a well-balanced diet that is low in calories and fat.
- orlistat capsules work by preventing the absorption of about 25% to 30% of the fat you eat. Instead of turning into calories, the fat passes out of your body.
- as a result of undigested fat passing through the body, you may experience bowel changes. Examples include fat in your stools and loose and more frequent stools, particularly after meals containing more fat than recommended.
- these bowel changes are related to how the product works and usually subside in a few weeks. You can decrease the likelihood of these effects by reducing the fat in your diet.
- you should start to lose weight within the first two weeks. How much weight you lose will depend on how closely you follow the recommended diet and the orlistat program.

If pregnant or breast-feeding, do not use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- for overweight adults 18 years and older
- before using this product, read the enclosed Companion Guide for complete directions and other important information
- 1 to 2 capsules with each meal containing fat. Start with 1 capsule. After you have gained experience with choosing meals that contain less than 30% fat, you can increase to 2 capsules for maximum weight loss.
- do not exceed 6 capsules daily
- continue daily use for up to 6 months. If you have not reached your weight loss goal by 6 months, talk to your doctor.
- to ensure adequate vitamin absorption, you should take a multivitamin once a day, 2 hours before or after taking orlistat capsules

Other information
- store at 20 – 25°C (68 – 77°F)
- avoid exposure to excessive light, humidity and temperatures over 30°C (86°F)

Inactive ingredients FD&C Blue No. 2, edible ink, gelatin, iron oxide, microcrystalline cellulose, povidone, sodium lauryl sulfate, sodium starch glycolate, talc, titanium dioxide

Questions or comments?
call **1-800-123-1234** weekdays (10:00 a.m. - 4:30 p.m. EST)
Llame a este numbero para obtener una copia de la etiqueta del producto en Espanol.

10.6 Table summarizing study design and results for the following randomized, placebo-controlled trials for orlistat: BM14149, BM14150, and NM17247

Studies to be submitted or referenced in support of the Orlistat 60 mg OTC NDA					
Study Protocol	**Study Period/ #subjects**	**BMI kg/m^2**	**Treatment Arms**	**Measured Outcome/Results**	**Additional Information**
BM14150	24 weeks	28 - 43	placebo TID 30 mg TID 60 mg TID 120 mg TID 240 mg TID	weight loss 30 mg not different from placebo (p=0.106) 60 mg, 120 mg, 240 mg showed statistically greater weight loss than placebo (p≤0.002)	Phase II, MC, DB, R, DD, PC, PD 4 week placebo lead-in period with subjects on a nutritionally balanced weight loss diet (600 kcal/day deficit) Clinic visits q 2 weeks for the first 2 months, then monthly. Mean weight loss compared to placebo: 30 mg = 0.95 kg 60 mg = 1.86 kg 120 mg = 2.55 kg 240 mg = 2.81 kg
NM17247	16 weeks 391 subjects 378 ITT 94% female 89% caucasian	25 to <28	placebo TID 60 mg TID	weight loss in subjects Placebo subtracted mean weight change from baseline: -1.15 kg (p<0.001)	R, DB, PC, PD, MC Primary care setting: mildly reduced calorie diet, no dietary counseling, or behavior modification. Additional 14 days of follow-up. Final telephone contact 14 days after the last dose of study medication.

Studies to be submitted or referenced in support of the Orlistat 60 mg OTC NDA

Study Protocol	Study Period/ #subjects	BMI kg/m^2	Treatment Arms	Measured Outcome/Results	Additional Information
BM14149	104 weeks 729 subjects 716 ITT "vast majority" female 99% caucasian	28 – 43	placebo TID 60 mg TID 120 mg TID	First year: weight loss with a 600 kcal/day deficit diet. After 24 weeks, caloric intake reduced by another 300 kcal/day. Second year: weight maintenance with a eucaloric diet. Mean weight loss, year 1: placebo 3.7 kg 120 mg 5.2 kg (p = 0.9) Mean percent weight loss from baseline: placebo -3.5% 60mg -5.6% 120mg -6.9% Mean weight loss, year 2: placebo 1.3 kg 60 mg 4.2 kg (p=0.01) 120 mg 5.2 kg (p<0.001)	Phase III, MC, DB, R, PD, DD, PC 4 week placebo lead-in period prior to 104 weeks of treatment. Overall weight management program: reduced calorie diet, dietary counseling, and behavior modification during the first year. Diet consisted of 3 meals/day with 30% fat, 50% carbohydrate, 20% protein, and a maximum of 300 mg/day cholesterol. Second year eucaloric diet: Caloric intake prescribed = estimated total daily energy expenditure (1.3 x BMR) minus 10% kcal/day. All groups lost about 3% of initial body weight during the 4 week placebo lead-in phase. All three treatment groups tended to regain weight during the second year of treatment. Mean levels of vitamins D, E, and β-carotene in the orlistat groups were reduced compared to placebo at weeks 52 and 104. Compared to placebo, orlistat significantly reduced total cholesterol, LDL-C, LDL/HDL ratio, BP, and glucose and attenuated the rise seen in these parameters during the second year of treatment.

11 REFERENCES

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Karen Feibus
3/6/2006 02:06:28 PM
MEDICAL OFFICER

see page 89, section7.2.2.2. Same comment added in exec sum and mentioned in recommendation.

Andrea Segal
3/6/2006 05:16:52 PM
MEDICAL OFFICER

Clinical Review

Completed date: 1/23/06

(for advisory committee background package)

Is located at:

http://www.fda.gov/ohrms/dockets/ac/cder06.html#EndocrinologicMetabolic

January 23, 2006 Joint Meeting with Nonprescription Drugs Advisory Committee

Briefing Information

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Memorandum from the Division of Pediatric Drug Development

Revised date: 12/28/05

Is located at:
http://www.fda.gov/ohrms/dockets/ac/cder06.html#EndocrinologicMetabolic

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Clinical Review

Completed date: 12/1/05

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