

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-362**

**ADMINISTRATIVE and CORRESPONDENCE**  
**DOCUMENTS**

**PATENT INFORMATION SUBMITTED UPON AND  
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

***For Each Patent That Claims a Drug Substance  
(Active Ingredient), Drug Product (Formulation or  
Composition) and/or Method of Use***

NDA NUMBER

22-362

NAME OF APPLICANT/NDA HOLDER

Daiichi Sankyo, Inc.

***The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.***

TRADE NAME

WELCHOL

ACTIVE INGREDIENT(S)

Colesevelam hydrochloride

STRENGTH(S)

Oral suspension: 3.75 gram packet, 1.875 gram packet

DOSAGE FORM

powder

APPROVAL DATE OF NDA OR SUPPLEMENT

October 2, 2009

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

**For hand-written or typewriter versions of this report:** If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

**FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.**

**For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.**

**1. GENERAL**

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
5,607,669	3/4/1997	6/10/2014
d. Name of Patent Owner	Address (of Patent Owner)	
Genzyme Corporation	500 Kendall Street	
	City/State	
	Cambridge, MA	
	ZIP Code	FAX Number (if available)
	02142	(617) 252-7600
	Telephone Number	E-Mail Address (if available)
	(617) 252-7500	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address (of agent or representative named in 1.e.)	
	City/State	
	ZIP Code	FAX Number (if available)
	Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

**2.1** Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☐ Yes ☒ No

**2.2** Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

**2.3** If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

**2.4** Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

**2.5** Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

**2.6** Does the patent claim only an intermediate? ☐ Yes ☒ No

**2.7** If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug substance if:**

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

**3.1** Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☐ Yes ☒ No

**3.2** Does the patent claim only an intermediate? ☐ Yes ☒ No

**3.3** If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug product if:**

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

**4.1** Does the patent claim one or more approved methods of using the approved drug product? ☒ Yes ☐ No

<b>4.2</b> Patent Claim Number(s) (as listed in the patent) 1, 2, 4 to 14, 18, and 20 to 25	Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
--	---

<b>4.2a</b> If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the approved labeling.) Under the heading INDICATIONS AND USAGE, it states "WELCHOL is indicated as an adjunct to diet and exercise to reduce elevated low-density lipoprotein cholesterol (LDL-C) in adults with primary hyperlipidemia . . . as monotherapy or in combination with . . . a (statin). WELCHOL is indicated as monotherapy or in combination with a statin to reduce LDL-C levels in [children 10-17]."
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<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.) <b>USE AS A BILE ACID SEQUESTRANT FOR LOWERING CHOLESTEROL</b>
FDA will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)  	Date Signed  10/28/2009
<b>NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</b>	
<b>Check applicable box and provide information below.</b>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Arthur Mann, Esq., Executive Director of Intellectual Property	
Address Daiichi Sankyo, Inc. Two Hilton Court	City/State Parsippany, NJ
ZIP Code 07054	Telephone Number 973-944-2623
FAX Number (if available) (973) 944-2808	E-Mail Address (if available) amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	

## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services Food and Drug Administration  <b>PATENT INFORMATION SUBMITTED UPON AND          AFTER APPROVAL OF AN NDA OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation or          Composition) and/or Method of Use</i>		Form Approved: OMB No. 0910-0513 Expiration Date: 7/31/10 See OMB Statement on Page 3.	
		NDA NUMBER	
		22-362	
		NAME OF APPLICANT/NDA HOLDER	
		Daiichi Sankyo, Inc.	
<b>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</b>			
TRADE NAME			
WELCHOL			
ACTIVE INGREDIENT(S)		STRENGTH(S)	
Colesevelam hydrochloride		Oral suspension: 3.75 gram packet, 1.875 gram packet	
DOSAGE FORM		APPROVAL DATE OF NDA OR SUPPLEMENT	
powder		October 2, 2009	
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.			
<b>For hand-written or typewriter versions of this report:</b> If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.			
<b>FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</b>			
<b>For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.</b>			
<b>1. GENERAL</b>			
a. United States Patent Number		b. Issue Date of Patent	c. Expiration Date of Patent
5,679,717		10/21/1997	4/29/2014
d. Name of Patent Owner		Address (of Patent Owner)	
Genzyme Corporation		500 Kendall Street	
		City/State	
		Cambridge, MA	
		ZIP Code	FAX Number (if available)
		02142	(617) 252-7600
		Telephone Number	E-Mail Address (if available)
		(617) 252-7500	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

**2.1** Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☐ Yes ☒ No

**2.2** Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

**2.3** If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

**2.4** Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

**2.5** Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

**2.6** Does the patent claim only an intermediate? ☐ Yes ☒ No

**2.7** If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug substance if:**

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes."
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

**3.1** Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☐ Yes ☒ No

**3.2** Does the patent claim only an intermediate? ☐ Yes ☒ No

**3.3** If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug product if:**

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

**4.1** Does the patent claim one or more approved methods of using the approved drug product? ☒ Yes ☐ No

<b>4.2</b> Patent Claim Number(s) (as listed in the patent) 1 to 5, 8 to 11, 16, 17, 22, 23, 27-36, and 40-46	Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
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<b>4.2a</b> If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the approved labeling.) Under the heading INDICATIONS AND USAGE, it states "WELCHOL is indicated as an adjunct to diet and exercise to reduce elevated low-density lipoprotein cholesterol (LDL-C) in adults with primary hyperlipidemia . . . as monotherapy or in combination with . . . a (statin). WELCHOL is indicated as monotherapy or in combination with a statin to reduce LDL-C levels in [children 10-17]."
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<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.) <b>USE AS A BILE ACID SEQUESTRANT FOR LOWERING CHOLESTEROL</b>
FDA will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)  	Date Signed  10/28/2009
<b>NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</b>	
<b>Check applicable box and provide information below.</b>	
<input type="checkbox"/> NDA Applicant/Holder  <input type="checkbox"/> Patent Owner	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official  <input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Arthur Mann, Esq., Executive Director of Intellectual Property	
Address Daiichi Sankyo, Inc. Two Hilton Court	City/State Parsippany, NJ
ZIP Code 07054	Telephone Number 973-944-2623
FAX Number (if available) (973) 944-2808	E-Mail Address (if available) amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	



## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
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- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

**PATENT INFORMATION SUBMITTED UPON AND  
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

***For Each Patent That Claims a Drug Substance  
(Active Ingredient), Drug Product (Formulation or  
Composition) and/or Method of Use***

NDA NUMBER

22-362

NAME OF APPLICANT/NDA HOLDER

Daiichi Sankyo, Inc.

***The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.***

TRADE NAME

WELCHOL

ACTIVE INGREDIENT(S)

Colesevelam hydrochloride

STRENGTH(S)

Oral suspension: 3.75 gram packet, 1.875 gram packet

DOSAGE FORM

powder

APPROVAL DATE OF NDA OR SUPPLEMENT

October 2, 2009

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

**For hand-written or typewriter versions of this report:** If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

***FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.***

***For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.***

**1. GENERAL**

a. United States Patent Number

5,693,675

b. Issue Date of Patent

12/2/1997

c. Expiration Date of Patent

12/2/2014

d. Name of Patent Owner

Genzyme Corporation

Address (of Patent Owner)

500 Kendall Street

City/State

Cambridge, MA

ZIP Code

02142

FAX Number (if available)

(617) 252-7600

Telephone Number

(617) 252-7500

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

Telephone Number

FAX Number (if available)

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

☒ Yes

☐ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

☐ Yes

☒ No

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

**2.1** Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☒ Yes ☐ No

**2.2** Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

**2.3** If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

**2.4** Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

**2.5** Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

**2.6** Does the patent claim only an intermediate? ☐ Yes ☒ No

**2.7** If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug substance if:**

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes."
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

**3.1** Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☐ Yes ☒ No

**3.2** Does the patent claim only an intermediate? ☐ Yes ☒ No

**3.3** If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug product if:**

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

**4.1** Does the patent claim one or more approved methods of using the approved drug product? ☐ Yes ☒ No

**4.2** Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? ☐ Yes ☐ No

**4.2a** If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)
FDA will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)	Date Signed
	10/28/2009
<b>NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</b>	
<b>Check applicable box and provide information below.</b>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<b>Name</b> Arthur Mann, Esq., Executive Director of Intellectual Property	
<b>Address</b> Daiichi Sankyo, Inc. Two Hilton Court	<b>City/State</b> Parsippany, NJ
<b>ZIP Code</b> 07054	<b>Telephone Number</b> 973-944-2623
<b>FAX Number (if available)</b> (973) 944-2808	<b>E-Mail Address (if available)</b> amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	

## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services Food and Drug Administration  <b>PATENT INFORMATION SUBMITTED UPON AND          AFTER APPROVAL OF AN NDA OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation or          Composition) and/or Method of Use</i>		Form Approved: OMB No. 0910-0513 Expiration Date: 7/31/10 See OMB Statement on Page 3.	
		NDA NUMBER	
		22-362	
		NAME OF APPLICANT/NDA HOLDER	
		Daiichi Sankyo, Inc.	
<b>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</b>			
TRADE NAME			
WELCHOL			
ACTIVE INGREDIENT(S)		STRENGTH(S)	
Colesevelam hydrochloride		Oral suspension: 3.75 gram packet, 1.875 gram packet	
DOSAGE FORM		APPROVAL DATE OF NDA OR SUPPLEMENT	
powder		October 2, 2009	
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.			
<b>For hand-written or typewriter versions of this report:</b> If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.			
<b>FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</b>			
<b>For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.</b>			
<b>1. GENERAL</b>			
a. United States Patent Number		b. Issue Date of Patent	c. Expiration Date of Patent
5,917,007		6/29/1999	4/29/2014
d. Name of Patent Owner Genzyme Corporation		Address (of Patent Owner)	
		500 Kendall Street	
		City/State	
		Cambridge, MA	
		ZIP Code	
		FAX Number (if available)	
		(617) 252-7600	
		E-Mail Address (if available)	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	
		FAX Number (if available)	
		E-Mail Address (if available)	
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☒ Yes ☐ No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

2.6 Does the patent claim only an intermediate? ☐ Yes ☒ No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug substance if:**

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☐ Yes ☒ No

3.2 Does the patent claim only an intermediate? ☐ Yes ☒ No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug product if:**

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more approved methods of using the approved drug product? ☒ Yes ☐ No

4.2 Patent Claim Number(s) (as listed in the patent) 62, 84, 91 to 95, and 98	Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
--	---

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.	<p>Use: (Submit indication or method of use information as identified specifically in the approved labeling.)</p> <p>Under the heading INDICATIONS AND USAGE, it states "WELCHOL is indicated as an adjunct to diet and exercise to reduce elevated low-density lipoprotein cholesterol (LDL-C) in adults with primary hyperlipidemia . . . as monotherapy or in combination with . . . a (statin). WELCHOL is indicated as monotherapy or in combination with a statin to reduce LDL-C levels in [children 10-17].</p>
---	---

<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.) <b>USE AS A BILE ACID SEQUESTRANT FOR LOWERING CHOLESTEROL</b>
FDA will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)  	Date Signed  10/28/2009
<b>NOTE:</b> Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).	
<b>Check applicable box and provide information below.</b>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Arthur Mann, Esq., Executive Director of Intellectual Property	
Address Daiichi Sankyo, Inc. Two Hilton Court	City/State Parsippany, NJ
ZIP Code 07054	Telephone Number 973-944-2623
FAX Number (if available) (973) 944-2808	E-Mail Address (if available) amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	



## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services Food and Drug Administration  <b>PATENT INFORMATION SUBMITTED UPON AND          AFTER APPROVAL OF AN NDA OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation or          Composition) and/or Method of Use</i>		Form Approved: OMB No. 0910-0513 Expiration Date: 7/31/10 See OMB Statement on Page 3.	
		NDA NUMBER	
		22-362	
		NAME OF APPLICANT/NDA HOLDER	
		Daiichi Sankyo, Inc.	
<b>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</b>			
TRADE NAME			
WELCHOL			
ACTIVE INGREDIENT(S)		STRENGTH(S)	
Colesevelam hydrochloride		Oral suspension: 3.75 gram packet, 1.875 gram packet	
DOSAGE FORM		APPROVAL DATE OF NDA OR SUPPLEMENT	
powder		October 2, 2009	
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.			
<b>For hand-written or typewriter versions of this report:</b> If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.			
<b>FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</b>			
<b>For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.</b>			
<b>1. GENERAL</b>			
a. United States Patent Number		b. Issue Date of Patent	c. Expiration Date of Patent
5,919,832		7/6/1999	4/29/2014
d. Name of Patent Owner		Address (of Patent Owner)	
Genzyme Corporation		500 Kendall Street	
		City/State	
		Cambridge, MA	
		ZIP Code	FAX Number (if available)
		02142	(617) 252-7600
		Telephone Number	E-Mail Address (if available)
		(617) 252-7500	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☒ Yes ☐ No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

2.6 Does the patent claim only an intermediate? ☐ Yes ☒ No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug substance if:**

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes."
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☐ Yes ☒ No

3.2 Does the patent claim only an intermediate? ☐ Yes ☒ No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug product if:**

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more approved methods of using the approved drug product? ☐ Yes ☒ No

4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? ☐ Yes ☐ No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)
FDA will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>• the answer to question 4.1 or 4.2 is "No," or</li> <li>• if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)	Date Signed
	10/28/2009
<b>NOTE:</b> Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).	
<b>Check applicable box and provide information below.</b>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<b>Name</b> Arthur Mann, Esq., Executive Director of Intellectual Property	
<b>Address</b> Daiichi Sankyo, Inc. Two Hilton Court	<b>City/State</b> Parsippany, NJ
<b>ZIP Code</b> 07054	<b>Telephone Number</b> 973-944-2623
<b>FAX Number (if available)</b> (973) 944-2808	<b>E-Mail Address (if available)</b> amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	

## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services Food and Drug Administration  <b>PATENT INFORMATION SUBMITTED UPON AND          AFTER APPROVAL OF AN NDA OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation or          Composition) and/or Method of Use</i>		Form Approved: OMB No. 0910-0513 Expiration Date: 7/31/10 See OMB Statement on Page 3.	
		NDA NUMBER	
		22-362	
		NAME OF APPLICANT/NDA HOLDER	
		Daiichi Sankyo, Inc.	
<b>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</b>			
TRADE NAME			
WELCHOL			
ACTIVE INGREDIENT(S)		STRENGTH(S)	
Colesevelam hydrochloride		Oral suspension: 3.75 gram packet, 1.875 gram packet	
DOSAGE FORM		APPROVAL DATE OF NDA OR SUPPLEMENT	
powder		October 2, 2009	
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.			
<b>For hand-written or typewriter versions of this report:</b> If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.			
<b>FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</b>			
<b>For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.</b>			
<b>1. GENERAL</b>			
a. United States Patent Number		b. Issue Date of Patent	
6,066,678		5/23/2000	
		c. Expiration Date of Patent	
		4/29/2014	
d. Name of Patent Owner		Address (of Patent Owner)	
Genzyme Corporation		500 Kendall Street	
		City/State	
		Cambridge, MA	
		ZIP Code	FAX Number (if available)
		02142	(617) 252-7600
		Telephone Number	E-Mail Address (if available)
		(617) 252-7500	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input checked="checked" type="checkbox"/> Yes <input type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input checked="checked" type="checkbox"/> No	

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☒ Yes ☐ No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

2.6 Does the patent claim only an intermediate? ☐ Yes ☒ No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

FDA will not list the patent in the Orange Book as claiming the drug substance if:

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes."
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☐ Yes ☒ No

3.2 Does the patent claim only an intermediate? ☐ Yes ☒ No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

FDA will not list the patent in the Orange Book as claiming the drug product if:

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more approved methods of using the approved drug product? ☒ Yes ☐ No

4.2 Patent Claim Number(s) (as listed in the patent) 13 to 24 Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? ☒ Yes ☐ No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

Under the heading INDICATIONS AND USAGE, it states "WELCHOL is indicated as an adjunct to diet and exercise to reduce elevated low-density lipoprotein cholesterol (LDL-C) in adults with primary hyperlipidemia . . . as monotherapy or in combination with . . . a (statin). WELCHOL is indicated as monotherapy or in combination with a statin to reduce LDL-C levels in [children 10-17].



<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.) <b>USE AS A BILE ACID SEQUESTRANT FOR LOWERING CHOLESTEROL</b>
<b>FDA will not list the patent in the Orange Book as claiming the method of use if:</b> <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)  <div style="text-align: center; font-family: cursive; font-size: 1.2em;">Arthur Mann</div>	Date Signed  10/28/2009
<b>NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</b>	
<b>Check applicable box and provide information below.</b>	
<input type="checkbox"/> NDA Applicant/Holder  <input type="checkbox"/> Patent Owner	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official  <input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<b>Name</b> Arthur Mann, Esq., Executive Director of Intellectual Property	
<b>Address</b> Daiichi Sankyo, Inc. Two Hilton Court	<b>City/State</b> Parsippany, NJ
<b>ZIP Code</b> 07054	<b>Telephone Number</b> 973-944-2623
<b>FAX Number (if available)</b> (973) 944-2808	<b>E-Mail Address (if available)</b> amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	



## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

**PATENT INFORMATION SUBMITTED UPON AND  
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

***For Each Patent That Claims a Drug Substance  
(Active Ingredient), Drug Product (Formulation or  
Composition) and/or Method of Use***

NDA NUMBER

22-362

NAME OF APPLICANT/NDA HOLDER

Daiichi Sankyo, Inc.

***The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.***

TRADE NAME

WELCHOL

ACTIVE INGREDIENT(S)

Colesevelam hydrochloride

STRENGTH(S)

Oral suspension: 3.75 gram packet, 1.875 gram packet

DOSAGE FORM

powder

APPROVAL DATE OF NDA OR SUPPLEMENT

October 2, 2009

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

**For hand-written or typewriter versions of this report:** If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

***FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.***

***For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.***

**1. GENERAL**

a. United States Patent Number 6,433,026	b. Issue Date of Patent 8/13/2002	c. Expiration Date of Patent 4/29/2014
d. Name of Patent Owner Genzyme Corporation	Address (of Patent Owner) 500 Kendall Street	
	City/State Cambridge, MA	
	ZIP Code 02142	FAX Number (if available) (617) 252-7600
	Telephone Number (617) 252-7500	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address (of agent or representative named in 1.e.)	
	City/State	
	ZIP Code	FAX Number (if available)
	Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☒ Yes ☐ No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

2.6 Does the patent claim only an intermediate? ☐ Yes ☒ No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug substance if:**

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☐ Yes ☒ No

3.2 Does the patent claim only an intermediate? ☐ Yes ☒ No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug product if:**

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more approved methods of using the approved drug product? ☐ Yes ☒ No

4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? ☐ Yes ☐ No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)
FDA will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)  <div style="font-family: cursive; font-size: 1.2em; color: blue;">Arthur Mann</div>	Date Signed  10/28/2009
<b>NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</b>	
<b>Check applicable box and provide information below.</b>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Arthur Mann, Esq., Executive Director of Intellectual Property	
Address Daiichi Sankyo, Inc. Two Hilton Court	City/State Parsippany, NJ
ZIP Code 07054	Telephone Number 973-944-2623
FAX Number (if available) (973) 944-2808	E-Mail Address (if available) amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	

## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services Food and Drug Administration  <b>PATENT INFORMATION SUBMITTED UPON AND          AFTER APPROVAL OF AN NDA OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation or          Composition) and/or Method of Use</i>		Form Approved: OMB No. 0910-0513 Expiration Date: 7/31/10 See OMB Statement on Page 3.	
		NDA NUMBER	
		22-362	
		NAME OF APPLICANT/NDA HOLDER	
		Daiichi Sankyo, Inc.	
<b>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</b>			
TRADE NAME			
WELCHOL			
ACTIVE INGREDIENT(S)		STRENGTH(S)	
Colesevelam hydrochloride		Oral suspension: 3.75 gram packet, 1.875 gram packet	
DOSAGE FORM		APPROVAL DATE OF NDA OR SUPPLEMENT	
powder		October 2, 2009	
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.			
<b>For hand-written or typewriter versions of this report:</b> If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.			
<b>FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</b>			
<b>For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.</b>			
<b>1. GENERAL</b>			
a. United States Patent Number		b. Issue Date of Patent	
6,784,254		8/31/2004	
		c. Expiration Date of Patent	
		4/29/2014	
d. Name of Patent Owner		Address (of Patent Owner)	
Genzyme Corporation		500 Kendall Street	
		City/State	
		Cambridge, MA	
		ZIP Code	FAX Number (if available)
		02142	(617) 252-7600
		Telephone Number	E-Mail Address (if available)
		(617) 252-7500	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

**2.1** Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☒ Yes ☐ No

**2.2** Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

**2.3** If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

**2.4** Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

**2.5** Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

**2.6** Does the patent claim only an intermediate? ☐ Yes ☒ No

**2.7** If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug substance if:**

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes."
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

**3.1** Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☒ Yes ☐ No

**3.2** Does the patent claim only an intermediate? ☐ Yes ☒ No

**3.3** If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug product if:**

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

**4.1** Does the patent claim one or more approved methods of using the approved drug product? ☐ Yes ☒ No

**4.2** Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? ☐ Yes ☐ No

**4.2a** If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)



<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.)
FDA will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)  	Date Signed  10/28/2009
<b>NOTE:</b> Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).	
Check applicable box and provide information below.	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Arthur Mann, Esq., Executive Director of Intellectual Property	
Address Daiichi Sankyo, Inc. Two Hilton Court	City/State Parsippany, NJ
ZIP Code 07054	Telephone Number 973-944-2623
FAX Number (if available) (973) 944-2808	E-Mail Address (if available) amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	



## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services Food and Drug Administration  <b>PATENT INFORMATION SUBMITTED UPON AND          AFTER APPROVAL OF AN NDA OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation or          Composition) and/or Method of Use</i>		Form Approved: OMB No. 0910-0513 Expiration Date: 7/31/10 See OMB Statement on Page 3.	
		NDA NUMBER	
		22-362	
		NAME OF APPLICANT/NDA HOLDER	
		Daiichi Sankyo, Inc.	
<b>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</b>			
TRADE NAME			
WELCHOL			
ACTIVE INGREDIENT(S)		STRENGTH(S)	
Colesevelam hydrochloride		Oral suspension: 3.75 gram packet, 1.875 gram packet	
DOSAGE FORM		APPROVAL DATE OF NDA OR SUPPLEMENT	
powder		October 2, 2009	
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.			
<b>For hand-written or typewriter versions of this report:</b> If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.			
<b>FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</b>			
<b>For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.</b>			
<b>1. GENERAL</b>			
a. United States Patent Number		b. Issue Date of Patent	c. Expiration Date of Patent
7,101,960		9/5/2006	4/29/2014
d. Name of Patent Owner Genzyme Corporation		Address (of Patent Owner)	
		500 Kendall Street	
		City/State	
		Cambridge, MA	
		ZIP Code	FAX Number (if available)
		02142	(617) 252-7600
		Telephone Number	E-Mail Address (if available)
		(617) 252-7500	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☒ Yes ☐ No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

2.6 Does the patent claim only an intermediate? ☐ Yes ☒ No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug substance if:**

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes,"
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☒ Yes ☐ No

3.2 Does the patent claim only an intermediate? ☐ Yes ☒ No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug product if:**

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more approved methods of using the approved drug product? ☒ Yes ☐ No

4.2 Patent Claim Number(s) (as listed in the patent) 13 to 18 Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? ☒ Yes ☐ No

4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)  
Under the heading INDICATIONS AND USAGE, it states "WELCHOL is indicated as an adjunct to diet and exercise to reduce elevated low-density lipoprotein cholesterol (LDL-C) in adults with primary hyperlipidemia . . . as monotherapy or in combination with . . . a (statin). WELCHOL is indicated as monotherapy or in combination with a statin to reduce LDL-C levels in [children 10-17]."

<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.) <b>USE AS A BILE ACID SEQUESTRANT FOR LOWERING CHOLESTEROL</b>
FDA will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)  	Date Signed  10/28/2009
<b>NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</b>	
<b>Check applicable box and provide information below.</b>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Arthur Mann, Esq., Executive Director of Intellectual Property	
Address Daiichi Sankyo, Inc. Two Hilton Court	City/State Parsippany, NJ
ZIP Code 07054	Telephone Number 973-944-2623
FAX Number (if available) (973) 944-2808	E-Mail Address (if available) amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	

## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

Department of Health and Human Services Food and Drug Administration  <b>PATENT INFORMATION SUBMITTED UPON AND          AFTER APPROVAL OF AN NDA OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation or          Composition) and/or Method of Use</i>		Form Approved: OMB No. 0910-0513 Expiration Date: 7/31/10 See OMB Statement on Page 3.	
		NDA NUMBER 22-362	
		NAME OF APPLICANT/NDA HOLDER Daiichi Sankyo, Inc.	
<b>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</b>			
TRADE NAME WELCHOL			
ACTIVE INGREDIENT(S) Colesevelam hydrochloride		STRENGTH(S) Oral suspension: 3.75 gram packet, 1.875 gram packet	
DOSAGE FORM powder		APPROVAL DATE OF NDA OR SUPPLEMENT October 2, 2009	
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.			
<b>For hand-written or typewriter versions of this report:</b> If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.			
<b>FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</b>			
<b>For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 and 6.</b>			
<b>1. GENERAL</b>			
a. United States Patent Number 7,229,613		b. Issue Date of Patent 6/12/2007	
		c. Expiration Date of Patent 4/17/2022	
d. Name of Patent Owner Genzyme Corporation		Address (of Patent Owner) 500 Kendall Street	
		City/State Cambridge, MA	
		ZIP Code 02142	FAX Number (if available) (617) 252-7600
		Telephone Number (617) 252-7500	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

## 2. Drug Substance (Active Ingredient)

**2.1** Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement? ☐ Yes ☒ No

**2.2** Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA? ☐ Yes ☒ No

**2.3** If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). ☐ Yes ☐ No

**2.4** Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

**2.5** Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.) ☐ Yes ☒ No

**2.6** Does the patent claim only an intermediate? ☐ Yes ☒ No

**2.7** If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug substance if:**

- the answers to 2.1 and 2.2 are "No," or,
- the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,
- the answer to 2.3 is "Yes" and there is no response to 2.4, or,
- the answer to 2.5 or 2.6 is "Yes."
- the answer to 2.7 is "No."

## 3. Drug Product (Composition/Formulation)

**3.1** Does the patent claim the approved drug product as defined in 21 CFR 314.3? ☐ Yes ☒ No

**3.2** Does the patent claim only an intermediate? ☐ Yes ☒ No

**3.3** If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) ☐ Yes ☐ No

**FDA will not list the patent in the Orange Book as claiming the drug product if:**

- the answer to question 3.1 is "No," or,
- the answer to question 3.2 is "Yes," or,
- the answer to question 3.3 is "No."

## 4. Method of Use

**Sponsors must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. For each approved method of use claimed by the patent, provide the following information:**

**4.1** Does the patent claim one or more approved methods of using the approved drug product? ☒ Yes ☐ No

<b>4.2</b> Patent Claim Number(s) (as listed in the patent) 1 to 4	Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
---	---

<b>4.2a</b> If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the approved labeling.) Under the heading INDICATIONS AND USAGE, it states WELCHOL "is indicated as an adjunct to diet and exercise to . . . improve glycemic control in adults with type 2 diabetes mellitus."
--	---



<b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.	Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.) <b>TREATMENT OF TYPE 2 DIABETES MELLITUS</b>
FDA will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>	
<b>5. No Relevant Patents</b>	
For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input type="checkbox"/> Yes</span>	
<b>6. Declaration Certification</b>	
<b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i>  <b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>	
<b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)  	Date Signed  10/28/2009
<b>NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</b>	
<b>Check applicable box and provide information below.</b>	
<input type="checkbox"/> NDA Applicant/Holder  <input type="checkbox"/> Patent Owner	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official  <input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Arthur Mann, Esq., Executive Director of Intellectual Property	
Address Daiichi Sankyo, Inc. Two Hilton Court	City/State Parsippany, NJ
ZIP Code 07054	Telephone Number 973-944-2623
FAX Number (if available) (973) 944-2808	E-Mail Address (if available) amann@dsi.com
<p>The public reporting burden for this collection of information has been estimated to average 5 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services          Food and Drug Administration          Office of Chief Information Officer (HFA-710)          5600 Fishers Lane          Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	



## INFORMATION AND INSTRUCTIONS FOR FORM 3542

### PATENT INFORMATION SUBMITTED UPON AND AFTER APPROVAL OF AN NDA OR SUPPLEMENT

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use. Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.
- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

#### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the approved NDA or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be listed. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be listed as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

#### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the approved NDA or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

#### 4. Method of Use

Complete all items in this section if the patent claims one or more methods of use of the drug product that is the subject of the approved NDA or supplement.

- 4.2) For each approved use of the drug claimed by the patent, identify by number the claim(s) in the patent that claim the approved use of the drug. An applicant may list together multiple patent claim numbers and information for each approved method of use, if applicable. However, each approved method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the approved drug labeling that is claimed by the patent.
- 4.2b) The answer to this question will be what FDA uses to create a "use-code" for Orange Book publication. The use code designates a method of use patent that claims the approved indication or use of a drug product. Each approved use claimed by the patent should be separately identified in this section and contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method of use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval. Use a maximum of 240 characters for each "use code."

#### 5. No Relevant Patents

Complete this section only if applicable.

#### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

## EXCLUSIVITY SUMMARY

NDA # 22-362

SUPPL #

HFD # 510

Trade Name Welchol for Oral Suspension

Generic Name colesevelam

Applicant Name Daiichi Sankyo

Approval Date, If Known 6/24/09

### **PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?**

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☐ NO ☒

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, **EXPLAIN** why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES ☐ NO ☒

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES ☒ NO ☐

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

NO

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

## **PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES**

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES ☒ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 21-176 Welchol (colesevelam) Tablets

NDA# 21-141 Welchol (colesevalam) Capsules

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES ☐ NO ☒

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)  
IF "YES," GO TO PART III.

**PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS**

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of

summary for that investigation.

YES ☐ NO ☒

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES ☐ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES ☐ NO ☐

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES ☐ NO ☐

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES ☐ NO ☐

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1		!
IND #	YES <input type="checkbox"/>	! NO <input type="checkbox"/>
		! Explain:

Investigation #2		!
IND #	YES <input type="checkbox"/>	! NO <input type="checkbox"/>
		! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES ☐

Explain:

!

!

! NO ☐

! Explain:

Investigation #2

YES ☐

Explain:

!

!

! NO ☐

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ☐

NO ☐

If yes, explain:

=====

Name of person completing form: Kati Johnson

Title: Project Manager

Date: 10/1/09

Name of Office/Division Director signing form: Eric Colman, MD

Title: Deputy Division Director/Lipid Team Leader

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05



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

KATI JOHNSON  
10/02/2009

ERIC C COLMAN  
10/02/2009

# **MEMORANDUM**

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

**DATE:** 10/2/09

**TO:** NDA File

**FROM:** Kati Johnson, Project Manager

**SUBJECT:** Pediatric Page

**APPLICATION/DRUG:**    **NDA 22-362**  
                                  **Welchol (colesevelam HCL) for Oral Suspension**

This new (powder) formulation was approved 10/2/09. Because of a glitch with DARRTS, the Pediatric Page can not be archived. In the interim, I am attaching the Pediatric Page to this memorandum so that it can be archived into the database.

**PEDIATRIC PAGE**  
**(Complete for all filed original applications and efficacy supplements)**

NDA/BLA#: 22-362 Supplement Number: \_\_\_\_\_ NDA Supplement Type (e.g. SE5): \_\_\_\_\_

Division Name: DMEP PDUFA Goal Date: 6/15/09 Stamp Date: 8/15/2008

Proprietary Name: Welchol

Established/Generic Name: colesevelam

Dosage Form: (b) (4) for oral suspension

Applicant/Sponsor: Daiichi Sankyo

Indication(s) previously approved (please complete this question for supplements and Type 6 NDAs only):

(1) reduce elevated LDL-C in patients with primary hyperlipidemia as monotherapy or in combination with HMGCoA reductase inhibitor

(2) improve glycermic control in adults with type 2 diabetes mellitus

(3) \_\_\_\_\_

(4) \_\_\_\_\_

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 0-a new dosage form only

(Attach a completed Pediatric Page for each indication in current application.)

**Indication:** reduce elevated LDL-C in patients with primary hyperlipidemia as monotherapy or in combination with HMGCoA reductase inhibitor

**Q1:** Is this application in response to a PREA PMR? Yes Continue

No X Please proceed to Question 2.

If Yes, NDA/BLA#: \_\_\_\_\_ Supplement #: \_\_\_\_\_ PMR #: \_\_\_\_\_

Does the division agree that this is a complete response to the PMR?

☐ Yes. Please proceed to Section D.

☐ No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

**Q2:** Does this application provide for (If yes, please check all categories that apply and proceed to the next question):

(a) NEW ☐ active ingredient(s) (includes new combination); ☐ indication(s); ☐ dosage form; ☐ dosing regimen; or ☐ route of administration?\*

(b) ☐ No. PREA does not apply. **Skip to signature block.**

**\* Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.**

**Q3:** Does this indication have orphan designation?

☐ Yes. PREA does not apply. **Skip to signature block.**

XNo. Please proceed to the next question.

**Q4:** Is there a full waiver for all pediatric age groups for this indication (check one)?

☐ Yes: (Complete Section A.)

X No: Please check all that apply:

X Partial Waiver for selected pediatric subpopulations (Complete Sections B)

☐ Deferred for some or all pediatric subpopulations (Complete Sections C)

☐ Completed for some or all pediatric subpopulations (Complete Sections D)

☐ Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)

☐ Extrapolation in One or More Pediatric Age Groups (Complete Section F)

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

<b>Section A: Fully Waived Studies (for all pediatric age groups)</b>
---

Reason(s) for full waiver: **(check, and attach a brief justification for the reason(s) selected)**

☐ Necessary studies would be impossible or highly impracticable because:

☐ Disease/condition does not exist in children

☐ Too few children with disease/condition to study

☐ Other (e.g., patients geographically dispersed): \_\_\_\_\_

☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.

☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

☐ Justification attached.

*If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.*

**Section B: Partially Waived Studies (for selected pediatric subpopulations)**

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

*Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).*

			Reason (see below for further detail):				
		minimum	maximum	Not feasible <sup>#</sup>	Not meaningful therapeutic benefit <sup>*</sup>	Ineffective or unsafe <sup>†</sup>	Formulation failed <sup>Δ</sup>
X	Neonate	__ wk. __ mo.	__ wk. __ mo.	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
X	Other	__ yr. __ mo.	10yr. __ mo.	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? X No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? X No; ☐ Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief justification**):

**#** Not feasible:

X Necessary studies would be impossible or highly impracticable because:

☐ Disease/condition does not exist in children

X Too few children with disease/condition to study

☐ Other (e.g., patients geographically dispersed): \_\_\_\_\_

**\*** Not meaningful therapeutic benefit:

☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

**†** Ineffective or unsafe:

☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

**Δ** Formulation failed:

☐ Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.*)

X Justification attached.

**The requirement was waived due to the limited population. In addition, the tablet size may preclude small children being able to swallow them. Lastly, there are gastrointestinal tolerability issues that could potentially make it difficult to study small children**

*For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding*

study plans that have been deferred (if so, proceed to Sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

**Section C: Deferred Studies (for selected pediatric subpopulations).**

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification <sup>†</sup>
Population		minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Date studies are due (mm/dd/yy): _____							

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

\* Other Reason: \_\_\_\_\_

<sup>†</sup> Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

**Section D: Completed Studies (for some or all pediatric subpopulations).**

Pediatric subpopulation(s) in which studies have been completed (check below):

Population		minimum	maximum	PeRC Pediatric Assessment form attached?.	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
X	Other	10 yr. __ mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? X No; ☐ Yes.Are the indicated age ranges (above) based on Tanner Stage? X No; ☐ Yes.

*Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):**

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

*If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)**

*Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as*

**IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL ([cderpmhs@fda.hhs.gov](mailto:cderpmhs@fda.hhs.gov)) OR AT 301-796-0700.**

*pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.*

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:					
Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

*Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.*

*If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.*

This page was completed by:

*{See appended electronic signature page}*

Regulatory Project Manager

(Revised: 6/2008)

**NOTE: If you have no other indications for this application, you may delete the attachments from this document.**



**Attachment A**

(This attachment is to be completed for those applications with multiple indications only.)

**Indication #2:** improve glycemic control in adults with type 2 diabetes mellitus

**Q1:** Does this indication have orphan designation?

☐ Yes. PREA does not apply. **Skip to signature block.**

X No. Please proceed to the next question.

**Q2:** Is there a full waiver for all pediatric age groups for this indication (check one)?

Yes: (Complete Section A.)

X No: Please check all that apply:

X Partial Waiver for selected pediatric subpopulations (Complete Sections B)

X Deferred for some or all pediatric subpopulations (Complete Sections C)

☐ Completed for some or all pediatric subpopulations (Complete Sections D)

☐ Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)

☐ Extrapolation in One or More Pediatric Age Groups (Complete Section F)

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

<b>Section A:</b> Fully Waived Studies (for all pediatric age groups)
---

Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

☐ Necessary studies would be impossible or highly impracticable because:

☐ Disease/condition does not exist in children

☐ Too few children with disease/condition to study

☐ Other (e.g., patients geographically dispersed): \_\_\_\_\_

Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.

☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

*If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.*

**Section B: Partially Waived Studies (for selected pediatric subpopulations)**

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

*Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).*

			Reason (see below for further detail):				
		minimum	maximum	Not feasible <sup>#</sup>	Not meaningful therapeutic benefit <sup>*</sup>	Ineffective or unsafe <sup>†</sup>	Formulation failed <sup>Δ</sup>
X	Neonate	__ wk. __ mo.	__ wk. __ mo.	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
X	Other	__ yr. <u>1</u> mo.	<u>9</u> yr. <u>11</u> mo.	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? X No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? X No; ☐ Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief justification**):

**#** Not feasible:

X Necessary studies would be impossible or highly impracticable because:

☐ Disease/condition does not exist in children

X Too few children with disease/condition to study

☐ Other (e.g., patients geographically dispersed): \_\_\_\_\_

**\*** Not meaningful therapeutic benefit:

☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

**†** Ineffective or unsafe:

☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

**Δ** Formulation failed:

☐ Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.*)

☐ Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Section C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL ([cderpmps@fda.hhs.gov](mailto:cderpmps@fda.hhs.gov)) OR AT 301-796-0700.

drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F).. Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

**Justification:** According to information collected by the Centers for Disease Control and Prevention in 2005, about 176,500 people aged 20 years or younger have diabetes in the United States. This represents 0.22% of all people in this age group. Currently, children with type 2 diabetes are usually diagnosed at the age of 10 years or older and are in middle to late puberty. Reported cases of type 2 diabetes in children showed a peak age of diagnosis during the usual pubertal age period, although there have been individuals described who were diagnosed prepubertally. The mean age of diagnosis was between 12 and 16 years. In a recently published population-based observational survey conducted in the US (SEARCH for Diabetes in Youth Study), the incidence of type 2 diabetes was significantly higher in age groups 10-14 and in particular age group 15-19 years compared to only a few cases per 100,000 person-years diagnosed at the age below 10 years. Although epidemiological data is limited in children with Type 2 diabetes, the low prevalence of the disease in children below 10 years of age makes the conduct of pediatric studies in this age group impractical.

**Section C: Deferred Studies (for some or all pediatric subpopulations).**

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification †
Population		minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
X	Other	10 yr. 0 mo.	17 yr. 11 mo.	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Date studies are due (mm/dd/yy): 11/30/2015							

Are the indicated age ranges (above) based on weight (kg)? X No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? X No; ☐ Yes.

\* Other Reason: \_\_\_\_\_

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL ([cderpmhs@fda.hhs.gov](mailto:cderpmhs@fda.hhs.gov)) OR AT 301-796-0700.

conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

**Section D: Completed Studies (for some or all pediatric subpopulations).**

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

*Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):**

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:			
Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

*If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)**

*Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.*

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

*Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.*

***If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS or DARRTS as appropriate after clearance by PeRC.***

This page was completed by:

*{See appended electronic signature page}*

Regulatory Project Manager

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700**

(Revised: 6/2008)

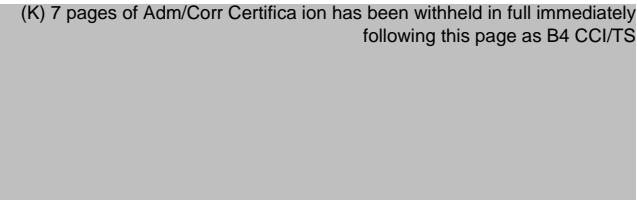
Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22362	ORIG-1	DAIICHI SANKYO INC	WELCHOL (b) (4) FOR ORAL SUSPENSION

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

/s/

KATI JOHNSON  
10/07/2009

(K) 7 pages of Adm/Corr Certification has been withheld in full immediately following this page as B4 CCI/TS



## ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION <sup>1</sup>		
NDA # 22-362 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Welchol Established/Proper Name: colesevelam Dosage Form: for Oral Suspension		Applicant: Daiichi Sankyo Agent for Applicant (if applicable):
RPM: Kati Johnson		Division: Metabolism and Endocrine
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><b><u>NDA's:</u></b>  NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1)   <input type="checkbox"/> 505(b)(2)  Efficacy Supplement:   <input type="checkbox"/> 505(b)(1)   <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> </div> <div style="width: 50%;"> <p><b><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></b>  Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p><b>Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.</b></p> <p style="text-align: center;"> <input type="checkbox"/> No changes                      <input type="checkbox"/> Updated  Date of check: </p> <p><b>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</b></p> <p><b>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</b></p> </div> </div>		
❖ User Fee Goal Date Action Goal Date (if different)		June 15, 2009
❖ Actions		
• Proposed action		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions ( <i>specify type and date for each action taken</i> )		X None
❖ Promotional Materials ( <i>accelerated approvals only</i> ) Note: If accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see guidance <a href="http://www.fda.gov/cder/guidance/2197dft.pdf">www.fda.gov/cder/guidance/2197dft.pdf</a> ). If not submitted, explain _____		<input type="checkbox"/> Received

<sup>1</sup> The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.



❖ Application <sup>2</sup> Characteristics		
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority          Chemical classification (new NDAs only):</p> <div style="display: flex; justify-content: space-between;"> <div> <input type="checkbox"/> Fast Track  <input type="checkbox"/> Rolling Review  <input type="checkbox"/> Orphan drug designation         </div> <div> <input type="checkbox"/> Rx-to-OTC full switch  <input type="checkbox"/> Rx-to-OTC partial switch  <input type="checkbox"/> Direct-to-OTC         </div> </div> <div style="display: flex; justify-content: space-between; margin-top: 10px;"> <div> <p>NDAs: Subpart H</p> <input type="checkbox"/> Accelerated approval (21 CFR 314.510)  <input type="checkbox"/> Restricted distribution (21 CFR 314.520)  <p>Subpart I</p> <input type="checkbox"/> Approval based on animal studies</div> <div> <p>BLAs: Subpart E</p> <input type="checkbox"/> Accelerated approval (21 CFR 601.41)  <input type="checkbox"/> Restricted distribution (21 CFR 601.42)  <p>Subpart H</p> <input type="checkbox"/> Approval based on animal studies</div> </div> <p><input type="checkbox"/> Submitted in response to a PMR  <input type="checkbox"/> Submitted in response to a PMC</p> <p>Comments: _____</p>		
❖ Date reviewed by PeRC ( <i>required for approvals only</i> ) If PeRC review not necessary, explain: _____	6/24/09	
❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM ( <i>approvals only</i> )	<input type="checkbox"/> Yes, date	
❖ BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 ( <i>approvals only</i> )	<input type="checkbox"/> Yes <input type="checkbox"/> No	
❖ Public communications ( <i>approvals only</i> )		
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
• Press Office notified of action (by OEP)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
• Indicate what types (if any) of information dissemination are anticipated	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other	

<sup>2</sup> All questions in all sections pertain to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
<ul style="list-style-type: none"> <li>Is approval of this application blocked by any type of exclusivity?</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> <li>NDA and BLA: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date 10-year limitation expires: _____
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> <li>Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.</li> </ul>	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> <li>Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.</li> </ul>	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> <li>[505(b)(2) applications] If the application includes a <b>paragraph III</b> certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).</li> </ul>	<input type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> <li>[505(b)(2) applications] For <b>each paragraph IV</b> certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i></li> </ul>	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

☐ Yes ☐ No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

*If "Yes," skip to question (4) below. If "No," continue with question (2).*

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

☐ Yes ☐ No

*If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.*

*If "No," continue with question (3).*

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

☐ Yes ☐ No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

*If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.*

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

☐ Yes ☐ No

*If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).*

*If "No," continue with question (5).*

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>CONTENTS OF ACTION PACKAGE</b>	
❖ Copy of this Action Package Checklist <sup>3</sup>	X
<b>Officer/Employee List</b>	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list ( <i>approvals only</i> )	X Included
Documentation of consent/non-consent by officers/employees	X Included
<b>Action Letters</b>	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date(s)
<b>Labeling</b>	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )	
<ul style="list-style-type: none"> <li>Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>	
<ul style="list-style-type: none"> <li>Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)</li> </ul>	
<ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>	X
<ul style="list-style-type: none"> <li>Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</li> </ul>	
❖ Medication Guide/Patient Package Insert/Instructions for Use ( <i>write submission/communication date at upper right of first page of each piece</i> )	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use X None

<sup>3</sup> Fill in blanks with dates of reviews, letters, etc.  
Version: 9/5/08

<ul style="list-style-type: none"> <li>Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>	
<ul style="list-style-type: none"> <li>Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)</li> </ul>	
<ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>	
<ul style="list-style-type: none"> <li>Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</li> </ul>	
❖ Labels ( <b>full color</b> carton and immediate-container labels) ( <i>write submission/communication date at upper right of first page of each submission</i> )	
<ul style="list-style-type: none"> <li>Most-recent division proposal for (only if generated after latest applicant submission)</li> </ul>	
<ul style="list-style-type: none"> <li>Most recent applicant-proposed labeling</li> </ul>	X
❖ Labeling reviews ( <i>indicate dates of reviews and meetings</i> )	<input type="checkbox"/> RPM X <input type="checkbox"/> DMEDP 4/28/09 <input type="checkbox"/> DRISK <input type="checkbox"/> DDMAC <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
❖ Proprietary Name <ul style="list-style-type: none"> <li>Review(s) (<i>indicate date(s)</i>)</li> <li>Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> </ul>	N/A
<b>Administrative / Regulatory Documents</b>	
❖ Administrative Reviews ( <i>e.g., RPM Filing Review<sup>4</sup>/Memo of Filing Meeting</i> ) ( <i>indicate date of each review</i> )	11/12/08
❖ NDAs only: Exclusivity Summary ( <i>signed by Division Director</i> )	X Included
❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ora/compliance_ref/aip_page.html">www.fda.gov/ora/compliance_ref/aip_page.html</a>	
<ul style="list-style-type: none"> <li>Applicant in on the AIP</li> </ul>	<input type="checkbox"/> Yes   X No
<ul style="list-style-type: none"> <li>This application is on the AIP <ul style="list-style-type: none"> <li>If yes, Center Director's Exception for Review memo (<i>indicate date</i>)</li> <li>If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes   X No  <input type="checkbox"/> Not an AP action
❖ Pediatric Page ( <i>approvals only, must be reviewed by PERC before finalized</i> )	X Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent ( <i>include certification</i> )	X Verified, statement is acceptable
❖ Postmarketing Requirement (PMR) Studies	X None
<ul style="list-style-type: none"> <li>Outgoing communications (<i>if located elsewhere in package, state where located</i>)</li> </ul>	
<ul style="list-style-type: none"> <li>Incoming submissions/communications</li> </ul>	
❖ Postmarketing Commitment (PMC) Studies	X None
<ul style="list-style-type: none"> <li>Outgoing Agency request for postmarketing commitments (<i>if located elsewhere in package, state where located</i>)</li> </ul>	

<sup>4</sup> Filing reviews for other disciplines should be filed behind the discipline tab.  
Version: 9/5/08

<ul style="list-style-type: none"> <li>Incoming submission documenting commitment</li> </ul>	
❖ Outgoing communications ( <i>letters (except previous action letters), emails, faxes, telecons</i> )	X
❖ Internal memoranda, telecons, etc.	N/A
❖ Minutes of Meetings	
<ul style="list-style-type: none"> <li>PeRC (<i>indicate date; approvals only</i>)</li> </ul>	<input type="checkbox"/> Not applicable 6/24/09
<ul style="list-style-type: none"> <li>Pre-Approval Safety Conference (<i>indicate date; approvals only</i>)</li> </ul>	<input type="checkbox"/> Not applicable
<ul style="list-style-type: none"> <li>Regulatory Briefing (<i>indicate date</i>)</li> </ul>	<input type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>Pre-NDA/BLA meeting (<i>indicate date</i>)</li> </ul>	X No mtg 3/13/08 clarification telecom re: 3/10/08 letter from FDA
<ul style="list-style-type: none"> <li>EOP2 meeting (<i>indicate date</i>)</li> </ul>	<input type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>Other (e.g., EOP2a, CMC pilot programs)</li> </ul>	
❖ Advisory Committee Meeting(s)	X No AC meeting
<ul style="list-style-type: none"> <li>Date(s) of Meeting(s)</li> </ul>	
<ul style="list-style-type: none"> <li>48-hour alert or minutes, if available</li> </ul>	
<b>Decisional and Summary Memos</b>	
❖ Office Director Decisional Memo ( <i>indicate date for each review</i> )	X None
Division Director Summary Review ( <i>indicate date for each review</i> )	X None
Cross-Discipline Team Leader Review ( <i>indicate date for each review</i> )	X None
<b>Clinical Information<sup>5</sup></b>	
❖ Clinical Reviews	
<ul style="list-style-type: none"> <li>Clinical Team Leader Review(s) (<i>indicate date for each review</i>)</li> </ul>	Concurred with 6/11/09 review
<ul style="list-style-type: none"> <li>Clinical review(s) (<i>indicate date for each review</i>)</li> </ul>	6/11/09
<ul style="list-style-type: none"> <li>Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)</li> </ul>	X None
❖ Safety update review(s) ( <i>indicate location/date if incorporated into another review</i> )	N/A
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, review/memo explaining why not	See page 4 of 6/11/09 clinical review
❖ Clinical reviews from other clinical areas/divisions/Centers ( <i>indicate date of each review</i> )	X None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation ( <i>indicate date of each review</i> )	X Not needed
❖ Risk Management <ul style="list-style-type: none"> <li>Review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)</li> <li>REMS Memo (<i>indicate date</i>)</li> <li>REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>)</li> </ul>	X None
❖ DSI Clinical Inspection Review Summary(ies) ( <i>include copies of DSI letters to investigators</i> )	X None requested
<b>Clinical Microbiology</b> <input type="checkbox"/> None	

<sup>5</sup> Filing reviews should be filed with the discipline reviews.  
Version: 9/5/08

❖ Clinical Microbiology Team Leader Review(s) <i>(indicate date for each review)</i>	X None
Clinical Microbiology Review(s) <i>(indicate date for each review)</i>	X None
<b>Biostatistics</b> <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) <i>(indicate date for each review)</i>	X None
Statistical Team Leader Review(s) <i>(indicate date for each review)</i>	X None
Statistical Review(s) <i>(indicate date for each review)</i>	X None
<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) <i>(indicate date for each review)</i>	X None
Clinical Pharmacology Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None concurred with 6/8/09 review
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>	6/8/09 None
❖ DSI Clinical Pharmacology Inspection Review Summary <i>(include copies of DSI letters)</i>	X None
<b>Nonclinical</b> <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) <i>(indicate date for each review)</i>	X None
• Supervisory Review(s) <i>(indicate date for each review)</i>	X None
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	X None
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer <i>(indicate date for each review)</i>	X None
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>	X <input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	X None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary <i>(include copies of DSI letters)</i>	X None requested
<b>CMC/Quality</b> <input type="checkbox"/> None	
❖ CMC/Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>	X None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None 6/11/09
• CMC/product quality review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None 6/10/09
• BLAs only: Facility information review(s) <i>(indicate dates)</i>	<input type="checkbox"/> None
❖ Microbiology Reviews	
• NDAs: Microbiology reviews (sterility & pyrogenicity) <i>(indicate date of each review)</i>	X <input type="checkbox"/> Not needed
• BLAs: Sterility assurance, product quality microbiology <i>(indicate date of each review)</i>	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	X None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	
X Review & FONSI <i>(indicate date of review)</i>	4/29/09

<input type="checkbox"/> Review & Environmental Impact Statement ( <i>indicate date of each review</i> )	
❖ NDAs: Methods Validation	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed
❖ Facilities Review/Inspection	
<ul style="list-style-type: none"> <li>• NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>)</li> </ul>	Date completed: 6/1/09 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<ul style="list-style-type: none"> <li>• BLAs:           <ul style="list-style-type: none"> <li>○ TBP-EER</li> <li>○ Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) (<i>date completed must be within 60 days prior to AP</i>)</li> </ul> </li> </ul>	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation Date completed: <input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold



## Appendix A to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication **AND** a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

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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.**  
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/s/  
-----

KATI JOHNSON  
10/01/2009



DAIICHI SANKYO PHARMA DEVELOPMENT  
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399 Thornall Street, Edison, NJ 08837  
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September 18, 2009

Mary Parks, M.D., Director  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705

**NDA 22-362**  
**Welchol® (colesevelam**  
**hydrochloride) for**  
**Oral Suspension**  
**eCTD Seq. 0008**

**Subject: Pediatric Plan for Welchol for Oral Suspension**

Dear Dr. Parks:

Reference is made to our New Drug Application, NDA 22-362 for Welchol® (colesevelam hydrochloride) for Oral Suspension. The original application, in eCTD format, was submitted to the Agency on August 15, 2008.

In response to an email we received from Ms. Kati Johnson on September 11, 2009, we are providing an updated pediatric plan which incorporates all of the comments included in that correspondence. Daiichi Sankyo commits to conduct a randomized, double-blind, two-arm trial that will include 200 T2DM patients ages 10-17. In order to blind the trial to the greatest extent possible, the doses used in the study, 0.625 g daily and 3.75 g daily, will be provided in identical packaging.

As previously discussed, Daiichi Sankyo is requesting a waiver for pediatric patients < 10 years of age.

We look forward to working with the Agency to finalize this pediatric plan and obtain regulatory approval for Welchol for Oral Suspension.

This submission has been prepared in accordance with ICH eCTD Specification 3.2, the final Guidance for Industry – “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Applications and Related Submissions using eCTD Specification, April 2006”, and the “Comprehensive Table of Contents Headings and Hierarchy, Version 1.2.”.

The electronic files have been checked with Symantec Antivirus Corporate Edition, Program Version 10.1.6.6000, Scan Engine 91.2.0.30, Virus Definition File 9/17/2009 rev. 2, and have been found to be virus free.



Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331 (j) as well as the FDA regulations.

If there should be any questions or need for additional information, please feel free to contact me via phone at 732-590-4986 or by email at [ggolikov@dsi.com](mailto:ggolikov@dsi.com).

Sincerely,

Gretchen Golikov  
Associate Director, Regulatory Affairs



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August 13, 2009

Mary Parks, M.D., Director  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705

**NDA 22-362**  
**Welchol® (colesevelam**  
**hydrochloride) for**  
**Oral Suspension**  
**eCTD Seq. 0007**

**Subject: Proposed Pediatric Plan for Welchol for Oral Suspension**

Dear Dr. Parks:

Reference is made to our New Drug Application, NDA 22-362 for Welchol® (colesevelam hydrochloride) for Oral Suspension. The original application, in eCTD format, was submitted to the Agency on August 15, 2008.

Thank you for the opportunity to discuss the path forward for the approval of the Welchol for Oral Suspension (OS) formulation during the teleconference on August 4, 2009. As discussed, Daiichi Sankyo (DSPD) is requesting a partial waiver for pediatric patients < 10 years of age and a deferral for conducting a trial in pediatric patients age 10-17 years of age.

As requested by the Pediatric Review Committee (PeRC), DSPD is amenable to conducting a clinical trial of Welchol OS in pediatric patients (age 10-17) with type 2 diabetes (T2DM). An outline of our proposed pediatric plan is attached. In reviewing our proposal, we would like you to consider the following background and rationale for our proposed study design.

- A pediatric study with Welchol tablets has already been completed in patients with hyperlipidemia; thus, there are data supporting the safety and efficacy of the drug in children. The study was conducted under a formal Written Request and additional product exclusivity was granted on February 17, 2009.
- The Written Request, Amendment 3 for pediatric patients with hyperlipidemia requires that *“if the studies you conduct in response to this Written Request demonstrate this drug will benefit children, then the age-appropriate dosage form must be made available for children.”* Welchol OS fulfills FDA’s request for development of an age appropriate formulation for children. In addition, the Welchol OS formulation will be useful to adult patients who have difficulty swallowing tablets.
- The safety and efficacy of Welchol tablets have been demonstrated in adults with T2DM, as add on to metformin, insulin or sulfonylurea-based treatment regimens. There is no reason to suspect that the course of the disease and the effects of the drug are different in adult and pediatric patients.

- Welchol is not absorbed systemically (and is not metabolized), and its mechanism of action has been demonstrated as valid in another pediatric indication (i.e., consistent with efficacy in adults). There is no reason to suspect the drug might behave differently in children, as opposed to adults, or pose a unique safety risk in pediatric patients.
- Welchol OS has been shown to be bioequivalent to Welchol tablets. Considering the pediatric study in hyperlipidemia, FDA concurred that it would be appropriate for the sponsor to request a pediatric waiver during the March 13, 2008, pre-NDA meeting for Welchol OS.

Applying these considerations to the FDA algorithm for determining the need for pediatric studies (see attached), DSPD proposes to perform a clinical study of the Welchol OS formulation in T2DM patients aged 10 to 17 years old. Briefly, the study would consist of a 2-arm, parallel-group trial evaluating the safety, tolerability and glycemic control imparted by a dose of Welchol anticipated to be subtherapeutic (0.625 mg daily), and the daily dose of Welchol recommended for adults (3.75 g). A matching or closely matching placebo is not feasible for the following reasons:

- Welchol powder for suspension is 75% active ingredient.
- An inert, insoluble replacement (excipient or polymer) having the same physiochemical and organoleptic characteristics (as colessevelam), in the demonstrated absence of glycemic or hypolipidemic effects, is not known. If identified, the substance would need to be safe at a dose of 2 to 3.5 g daily in a pediatric population; toxicological studies might be required. In addition, the substance would need to have demonstrated stability covering the period of the study, and hence would take a long time to develop.

The primary evaluation period will be 24 weeks, after which, all patients will be eligible to enter an approximately 6-month extension period on the full dose of Welchol (3.75 g daily). The key study objectives will be to demonstrate general safety and tolerability of Welchol OS in pediatric patients with T2DM, and to demonstrate the change from baseline in HbA1c for pediatric diabetes patients administered Welchol. A more detailed outline of the proposed study is attached.

Considering the scientific necessity and ability for extrapolation, discussed above, DSPD is also proposing this design out of feasibility concerns for recruiting a larger pediatric study in T2DM.

Despite the well-publicized rise in childhood obesity, the prevalence of T2DM in the pediatric population remains very low. The 1999-2002 National Health and Nutrition Examination Survey estimated 39,000 US adolescents (aged 12-19 years) with T2DM. The 2007 National Diabetes Statistics, maintained by NIDDK, estimated <200,000 patients with diabetes, inclusive of types 1 and 2, below the age of 20 years. Hence, based on this number, one can estimate a pediatric T2DM subpopulation of somewhere between 40,000 to 60,000.



In addition, currently, colesevelam is available in only a few ex-US countries, where it is labeled for the hyperlipidemia indication. DSPD only markets Welchol in the US; another sponsor, independent of DSPD, has rights to market colesevelam elsewhere. We face ethical challenges in attempts to enroll subjects, particularly children, from countries where the drug is not available (or will not be available), as DSPD would not be able to supply the drug to patients after the completion of the study. Lastly there are potential legal difficulties in regions where our studies would be conducted in territories marketed by the other sponsor.

On review of prior efforts, recruitment challenges are evident from the long timelines in other pediatric T2DM studies. A 200-subject study with rosiglitazone and metformin took more than 3 years to complete. Similarly, the NIH-sponsored TODAY trial just completed its enrollment after 4+years of recruitment. DSPD has had an opportunity to contact experts in pediatric diabetes who participated in these trials. They stressed the rarity of T2DM in children (4000 new cases per year in the US), and that the typical patient comes from a very challenging situation – one that creates great difficulties in initial identification, recruitment/enrollment and retention. (One or more of the experts we contacted can be made available to the Agency should this be of interest.)

The electronic files have been checked with Symantec Antivirus Corporate Edition, Program Version 10.1.6.6000, Scan Engine 81.3.0.13, Virus Definition File 8/11/2009, rev. 4, and have been found to be virus free.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331 (j) as well as the FDA regulations.

We look forward to working with the Agency to finalize the pediatric plan and obtain regulatory approval for Welchol Oral Suspension. If there should be any questions or need for additional information, please feel free to contact me via phone at 732-590-4984 or by email at [ssmith@dsi.com](mailto:ssmith@dsi.com). In my absence please contact Dr. Howard Hoffman at 732-590-5009 ([hhoffman@dsi.com](mailto:hhoffman@dsi.com)) or Gretchen Golikov at 732-590-4986 ([ggolikov@dsi.com](mailto:ggolikov@dsi.com)).

Sincerely,

Sandra Smith  
Senior Director, Regulatory Affairs



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June 23, 2009

Mary Parks, M.D., Director  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

**NDA Number 22-362**  
**Welchol® (colesevelam**  
**hydrochloride) for Oral Suspension**  
**eCTD Seq. 0006**

Dear Dr. Parks:

Reference is made to our New Drug Application, NDA 22-362 for Welchol® (colesevelam hydrochloride) for Oral Suspension. The original application, in eCTD format, was submitted to the Agency on August 15, 2008.

We are notifying the Agency that at this time we are

(b) (4)

This submission has been prepared in accordance with ICH eCTD Specification 3.2, the final Guidance for Industry – “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Applications and Related Submissions using eCTD Specification, April 2006”, and the “Comprehensive Table of Contents Headings and Hierarchy, Version 1.2.”.

The electronic files have been checked with Symantec Antivirus Corporate Edition, Program Version 10.1.6.6000, Scan Engine 81.3.0.13, Virus Definition File 6/22/2009 rev. 2, and have been found to be virus free.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331 (j) as well as the FDA regulations.

If there are any questions regarding this submission, please do not hesitate to call me at (732) 590-4986 or email me at [ggolikov@dsi.com](mailto:ggolikov@dsi.com).

Sincerely,

Gretchen Golikov  
Associate Director, Regulatory Affairs

cc: K. Johnson





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June 8, 2009

Mary Parks, M.D., Director  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705

**NDA 22-362**  
**Welchol® (colesevelam**  
**hydrochloride) (b) (4) for**  
**Oral Suspension**  
**eCTD Sequence No. 0005**

**Subject: Response to FDA Request for Bioequivalence Information**

Dear Dr. Parks:

Reference is made to our New Drug Application, NDA 22-362 for Welchol® (colesevelam hydrochloride) Powder for Oral Suspension. The original application, in eCTD format, was submitted to the Agency on August 15, 2008.

Reference is also made to the May 26 and June 1, 2009 email messages from Ms. K. Johnson, Project Management as well as the June 2nd teleconference regarding additional information requests from Dr. Vaidyanathan on the in vitro bioequivalence related matters. Provided in the attached is our [official electronic response](#) to the points identified which also includes information/data in the requested [Excel file](#) format.

All files were checked and verified to be free of viruses, prior to being submitted using Symantec Antivirus Corporate Edition, Program Version 10.1.6.6000, Scan Engine 81.3.0.13, and Virus Definition File 6/07/2009 rev. 4.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA regulations.

We trust the information provided satisfactorily addresses the issues discussed in the email messages and teleconference. Should there be any questions or need of further information, we will respond as quickly as possible. Please contact me directly by telephone at (732) 590-4875, by cell at (732) 512-8580, or by email at [pkosmoski@dsi.com](mailto:pkosmoski@dsi.com). In my absence, please feel free to contact Zoya Borodanski, Associate Director, Regulatory Affairs-CMC at (732) 590-4926.

Sincerely,

Paulette F. Kosmoski  
Executive Director, US/EU & Regional Regulatory Affairs-CMC

Enclosure

cc: Ms. K. Johnson  
Dr. J. Vaidyanathan  
Dr. W. Qiu



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May 22, 2009

Mary Parks, M.D., Director  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705

**NDA 22-362**  
**Welchol® (colesevelam**  
**hydrochloride) (b) (4) for**  
**Oral Suspension**  
**eCTD Sequence No. 0004**

**Subject: Response to FDA Request for Bioequivalence Information**

Dear Dr. Parks:

Reference is made to our New Drug Application, NDA 22-362 for Welchol® (colesevelam hydrochloride) (b) (4) for Oral Suspension. The original application, in eCTD format, was submitted to the Agency on August 15, 2008.

Reference is also made to the May 15 and 19, 2009 email messages from Ms. K. Johnson, Project Management regarding additional information requests from Dr. Vaidyanathan on the in vitro bioequivalence related matters. Provided in the attached is our official electronic response to the points identified in the aforementioned emails.

All electronic files included in this submission are approximately 600KB. All files were checked and verified to be free of viruses, prior to being submitted using Symantec Antivirus Corporate Edition, Program Version 10.1.6.6000, Scan Engine 81.3.0.13, and Virus Definition File 5/21/2009 rev. 3.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA regulations.

We trust the information provided satisfactorily addresses the issues discussed in the teleconference. Should there be any questions or need of further information, we will respond as quickly as possible. Please contact me directly by telephone at



(732) 590-4875, by cell at (732) 512-8580, or by email at [pkosmoski@dsi.com](mailto:pkosmoski@dsi.com). In my absence, please feel free to contact Zoya Borodanski, Associate Director, Regulatory Affairs-CMC at (732) 590-4926.

Sincerely,

Paulette F. Kosmoski  
Executive Director, US/EU & Regional Regulatory Affairs-CMC

Enclosure

cc: Ms. K. Johnson  
Dr. J. Vaidyanathan  
Dr. W. Qiu



DAIICHI SANKYO PHARMA  
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May 14, 2009

Mary Parks, M.D., Director  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705

NDA 22-362  
Welchol® (colesevelam  
hydrochloride) (b) (4) for  
Oral Suspension  
eCTD Sequence No. 0003

Subject: Response to FDA Request for CMC Information

Dear Dr. Parks:

Reference is made to our New Drug Application, NDA 22-362 for Welchol® (colesevelam hydrochloride) (b) (4) for Oral Suspension. The original application, in eCTD format, was submitted to the Agency on August 15, 2008.

Reference is also made to the May 8, 2009 teleconference held with Ms. K. Johnson, Project Management and Drs. A. Al-Hakim, E. Chikhale, M. Haber and S. Tran of ONDQA regarding additional information requests on the CMC related matters. Provided in this submission is our official electronic response to the points identified in the aforementioned teleconference.

In accordance with 21CFR314.70(a), a transmittal letter informing the New Jersey District Office of this CMC information amendment will be submitted to our home FDA district office in Parsippany, NJ concurrent with the electronic submission.

All electronic files included in this submission are approximately 1.92 MB. All files were checked and verified to be free of viruses, prior to being submitted using Symantec Antivirus Corporate Edition, Program Version 10.1.6.6000, Scan Engine 81.3.0.13, and Virus Definition File 5/13/2009 rev. 3.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA regulations.

We trust the information provided satisfactorily addresses the issues discussed in the teleconference. Should there be any questions or need of further information, we will

respond as quickly as possible. Please contact me directly by telephone at (732) 590-4875, by cell at (732) 512-8580, or by email at [pkosmoski@dsi.com](mailto:pkosmoski@dsi.com). In my absence, please feel free to contact Zoya Borodanski, Associate Director, Regulatory Affairs-CMC at (732) 590-4926.

Sincerely,

Paulette F. Kosmoski  
Executive Director, US/EU & Regional Regulatory Affairs-CMC

Enclosure

cc: Ms. K. Johnson  
Dr. E. Chikhale  
Dr. A.H. Al-Hakim  
Dr. S. Tran  
Dr. M. Haber



DAIICHI SANKYO PHARMA DEVELOPMENT  
a division of DAIICHI SANKYO, INC.

399 Thornall Street, Edison, NJ 08837  
Tel. 732 590 5000, Fax 732 906 5690

April 30, 2009

Mary Parks, M.D., Director  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705

NDA 22-362  
Welchol™ (colesevelam  
hydrochloride) (b) (4) for  
Oral Suspension  
eCTD Sequence No. 0002

**Subject: Response to FDA Request for CMC Information**

Dear Dr. Parks:

Reference is made to our New Drug Application, NDA 22-362 for Welchol® (colesevelam hydrochloride) (b) (4) for Oral Suspension. The original application, in eCTD format, was submitted to the Agency on August 15, 2008.

Reference is also made to two emails both dated April 16, 2009 from Ms. K. Johnson, Regulatory Project Manager regarding requests for additional information on three CMC matters. Provided in the attached is our official electronic response to the points identified in the aforementioned email requests to the pending NDA.

In accordance with 21CFR314.70(a), a transmittal letter informing the New Jersey District Office of this CMC information amendment will be submitted to our home FDA district office concurrent with the electronic submission.

All electronic files included in this submission are approximately 0.7 MB. All files were checked and verified to be free of viruses, prior to being submitted using Symantec Antivirus Corporate Edition, Program Version 8.1.0.825, Scan Version 4.2.0.7, and Virus Definition File 4/28/2009 rev. 3.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA regulations.



DAIICHI SANKYO PHARMA DEVELOPMENT  
a division of DAIICHI SANKYO, Inc.

399 Thornall Street, Edison, NJ 08837  
Tel. 732 590 5000, Fax 732 906 5690

December 8, 2008

Mary Parks, M.D., Director  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705

NDA 22-362  
Welchol® (colesevelam  
hydrochloride) (b) (4) for  
Oral Suspension  
eCTD Sequence No. 0001

Dear Dr. Parks:

Reference is made to our New Drug Application, NDA 22-362 for Welchol® (colesevelam hydrochloride) (b) (4) for Oral Suspension. The original application, in eCTD format, was submitted to the Agency on August 15, 2008.

In accordance with 21CFR314.600, we are hereby submitting a minor amendment to the pending NDA 22-362. This submission provides CMC information/data to:

- 1) update the stability program with 3 months real time and accelerated test data on demonstration batches produced at the (b) (4) (Report 7566-004); and
- 2) to include a statement of compliance with the standards of USP General Chapter <467>, Residual Solvents which became effective on July 1, 2008.

With regard to issue 1, please refer to the FDA minutes, issued March 19, 2008, of our March 13, 2008 pre-NDA meeting. It was agreed that the 3 month stability update would not constitute a major amendment affecting the PDUFA due date of June 15, 2009.

This electronic submission was prepared by a third party vendor, (b) (4) in accordance with ICH eCTD Specification 3.2., the final Guidance for Industry – “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Applications and Related Submissions using the eCTD Specification, April 2006”, and the “Comprehensive Table of Contents Heading and Hierarchy, Version 1.2.”

The electronic submission is approximately 2.3MB in size, and is in full eCTD format and provided via FDA’s Electronic Submission Gateway. It has been checked with Symantec Antivirus Corporate Edition, Program Version 8.1.0.825, Scan version 4.2.0.7, Virus Definition File 12/3/2008 rev. 04, and has been found to be virus free.

In accordance with 21CFR314.70(a), a transmittal letter informing the NJ District Office (Parsippany Resident Post) of this CMC information amendment is being submitted concurrently to our home FDA district office.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provision of 18 U.S.C., Section 190J or 210.U.S.C.331(j) as well as the FDA regulations.

If there are any questions or need of other information, please contact me at (732) 590-4875, fax at (732) 906-6652, or email at [pkosmoski@dsus.com](mailto:pkosmoski@dsus.com). In my absence, please contact Ms. Zoya Borodanski at (732) 590-4926. Thank you.

Sincerely,



Paulette F. Kosmoski  
Executive Director, US/EU & Regional Regulatory Affairs-CMC

Enclosures

cc: Ms. Kati Johnson (cover letter)





We trust the information provided satisfactorily addresses the issues outlined in the information request email. Should there be any questions or need of further information, we will respond as quickly as possible. Please contact me directly by telephone at (732) 590-4875, by cell at (732) 512-8580 or by email at [pkosmoski@dsus.com](mailto:pkosmoski@dsus.com). In my absence, please feel free to contact Zoya Borodanski, Associate Director, Regulatory Affairs-CMC at (732) 590-4926.

Sincerely,

Paulette F. Kosmoski  
Executive Director, US/EU & Regional Regulatory Affairs-CMC

Enclosure

Cc: Ms. K. Johnson  
Dr. E. Chikhale  
Dr. A.H. Al-Hakim



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 22-362

**NDA ACKNOWLEDGMENT**

Daiichi Sankyo, Inc.  
Attention: Paulette F. Kosmoski  
Executive Director, US/EU & Regional Regulatory Affairs-CMC  
399 Thornall Street  
Edison, NJ 08837

Dear Ms. Kosmoski:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Welchol (colesevelam HCL) (b) (4) for Oral Suspension

Date of Application: August 15, 2008

Date of Receipt: August 15, 2008

Our Reference Number: NDA 22-362

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on **October 14, 2008** in accordance with 21 CFR 314.101(a).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review

without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/cder/ddms/binders.htm>.

If you have any questions, call me at (301) 796-1234.

Sincerely,

*{See appended electronic signature page}*

Kati Johnson  
Project Manager  
Division of Metabolism and Endocrinology Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

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

/s/

-----  
Kati Johnson

8/28/2008 08:14:42 AM



DAIICHI SANKYO PHARMA  
a division of DAIICHI SANKYO, Inc.

399 Thornall Street, Edison, NJ 08837  
Tel. 732 590 5000, Fax 732 906 5690

August 15, 2008

Mary Parks, M.D., Director  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolism and Endocrinology Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Re: **INITIAL NEW DRUG APPLICATION**  
**NDA Number 22-362**  
**Welchol™ (colesevelam hydrochloride) (b) (4) for Oral Suspension**

Dear Dr. Parks:

In accordance with 21CFR314.50 and submitted under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, Daiichi Sankyo Pharma Development, a division of Daiichi Sankyo, Inc. (Daiichi Sankyo) is providing for submission of an original New Drug Application (NDA) for Welchol™ (colesevelam hydrochloride) (b) (4) for Oral Suspension. We are seeking approval of the (b) (4) for oral suspension as an alternate dosage form to the marketed Welchol™ tablets, NDA 21-176 and are proposing a single Welchol™ package insert based on the currently approved tablet labeling with appropriate sections modified to incorporate the (b) (4) for oral suspension dosage form.

Welchol™ (colesevelam hydrochloride) is a bile acid sequestrant and is indicated as an adjunct to diet and exercise to:

- ⊄ reduce elevated low density lipoprotein cholesterol (LDL-C) in patients with primary hypercholesterolemia as monotherapy or in combination with an hydroxymethylglutaryl-coenzyme A(HMG CoA) reductase inhibitor.
- ⊄ improve glycemic control in adults with type 2 diabetes mellitus.

This application relies in part on safety and efficacy information with relevant cross-reference to required Clinical, Nonclinical Pharmacology and Toxicology and Clinical Pharmacology elements in the approved NDAs for Welchol™ Tablets NDA 21-176 and Welchol™ Capsules NDA 21-141 as outlined in [Notes to Reviewers](#) attached to this cover letter.

Key interactions and agreements with the Agency during the course of development of Welchol™ (b) (4) for Oral Suspension are described in [Notes to Reviewers](#) with copies of related correspondence included in [Module 1.6.3](#) of this application.

This application is being submitted via the FDA Electronic Submission Gateway in electronic format according to *Guidance for Industry – Providing Regulatory Submissions in Electronic Format Human Pharmaceutical Product Applications and Related Submission Using eCTD Specification* (April, 2006). The size of the submission is approximately 100MB. All electronic files have been checked for viruses using Norton AntiVirus Program version: 8.1.0.825, Scan version 4.2.0.7, and Virus Definition file 8/12/2008, revision 3 and verified to be free of known viruses.

The NDA number 22-362 for the application was pre-assigned on March 27, 2008. The User Fee of \$589,000 for the application has been paid under User Fee Number PD3008525. Prescription Drug User Fee cover sheet, form FDA 3397 has been provided in [Module 1.1.3](#). This application does not contain clinical data.

The official contacts for this application at Daiichi Sankyo Pharma Development, 399 Thornall Street, Edison, NJ 08837 are:

Paulette F. Kosmoski  
Executive Director, US/EU & Regional Regulatory Affairs-CMC  
Telephone: 732-590-4875  
Fax: 732-906-6652  
Cell: 732-512-8580  
Email: [pkosmoski@dsus.com](mailto:pkosmoski@dsus.com)

In the case of Ms. Kosmoski's absence, please contact:

Zoya Borodanski  
Associate Director, Regulatory Affairs-CMC  
Telephone: 732-590-4926  
Fax: 732-906-6652  
Cell: 917-399-8689  
Email: [zborodanski@dsus.com](mailto:zborodanski@dsus.com)

Please direct any questions relating to labeling to:

Gretchen Golikov  
Associate Director, Regulatory Affairs  
Telephone: 1-732-590-4986  
Fax: 732-906-6652  
Email: [ggolikov@dsus.com](mailto:ggolikov@dsus.com)

Daiichi Sankyo considers the information contained in this application to be confidential and its contents are not to be disclosed without express written consent.



## **Notes to FDA Reviewers**

### **NDA 22-362**

#### **Introduction**

Daiichi Sankyo Pharma Development (DSPD), a division of Daiichi Sankyo Inc., is submitting this New Drug Application to gain approved for Welchol™ (colesevelam hydrochloride) (b) (4) for Oral Suspension for the following indication:

Welchol™ (colesevelam hydrochloride) is a bile acid sequestrant indicated as an adjunct to diet and exercise to

- € reduce elevated low-density lipoprotein cholesterol (LDL-C) in patients with primary hyperlipidemia as monotherapy or in combination with an hydroxymethyl-glutaryl-coenzyme A (HMG CoA) reductase inhibitor.
- € improve glycemic control in adults in type 2 diabetes mellitus.

This “Notes to Reviewers” highlights specific aspects of the NDA that we wish to emphasize.

It covers the following topics:

- € Submission information, including Format and Organization
- € Details Regarding Specific Application Modules
- € Documents that will be provided after NDA submission
- € Regulatory History and Agreements



## **Submission Information, including Format and Organization**

This application is formatted and organized according to 21 CFR 314.50 and follows the *M4: Common Technical Document for the Registration of Pharmaceuticals for Use*. This application is being submitted in electronic format according to *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submission using the eCTD Specifications* (April, 2006).

All electronic media have been checked and verified to be free of known viruses with the most current version of Symantec Antivirus Program.

## **Details Regarding Specific Application Modules**

This section provides a summary of key items of note for the FDA reviewers by Module of the eCTD. The sponsors have discussed many of the content and format elements of this submission with the FDA ([see Regulatory History](#)).

### **Module 1**

The following is a summary of the documents included in Module 1 of this submission:

- € Copies of the proposed labeling ([annotated](#) and [unannotated](#)) for Welchol™ for the existing indications are in this Module. Copies of [packet labels](#) and [primary carton labeling](#) are located in this Module.
- € All referenced FDA communications, major submissions and FDA and sponsor's meeting minutes are provided in [Module 1.6.3](#).
- € [Debarment certification](#), [patent certifications](#), [environmental assessment](#), [FDA form 3674](#) and [FDA form 356h](#) are provided in this Module.
- € The [User Fee](#), payment of \$589,000 for the application was provided on July 23, 2008, PD3008525. The application does not contain clinical data as there were no clinical studies.
- € A [request for pediatric waiver](#) is provided.

€ A note of intent to file a [petition to the Consumer Product Safety Commission](#) to exempt Welchol™ (b) (4) for Oral Suspension from the requirements of the Poison Prevention Packaging Act is provided.

€ Risk Evaluation and Mitigation Strategy (REMS) is not provided in the submission based on agreement by FDA as reflected in FDA meeting minutes.

€ As there were no clinical studies conducted with Welchol™ (b) (4) for Oral Suspension, investigator financial disclosure information is not applicable.

## **Module 2**

All Clinical, Nonclinical Pharmacology and Toxicology, Clinical Pharmacology required elements such as related summaries and overviews are cross referenced to the approved NDAs for capsule and tablet formulations of Welchol™, NDA 21-141 and NDA 21-176, respectively.

A [summary of the \*in-vitro\* bioequivalence study](#) comparing the proposed Welchol™ (b) (4) for Oral Suspension to the marketed tablet formulation is provided in this Module.

This Module contains the [Quality Overall Summary](#) which provides an overview of key development considerations for the drug product.

### **Module 3 (Chemistry)**

Module 3 includes the chemistry, manufacturing and controls information for the drug substance (colesevelam hydrochloride) and drug product ((b) (4) for oral suspension). Information pertaining to the drug substance is mainly provided by cross reference to NDA 21-141 and NDA 21-176. [Field copy certification](#) is being provided simultaneously to Daiichi Sankyo's home FDA District Office in North Brunswick, New Jersey. Daiichi Sankyo affirms that all manufacturing and testing sites listed in this application that are involved in the commercial manufacturing, packaging and testing of Welchol™ are available for [pre-approval inspection](#).

### **Module 4 (Nonclinical Pharmacology and Toxicology)**

All nonclinical pharmacology, toxicology and ADME information elements specific to colesevelam hydrochloride are provided by cross reference to the approved NDAs for capsule and tablet formulations of Welchol™, NDA 21-141 and NDA 21-176, respectively.

### **Module 5 (Clinical)**

All Clinical required elements to include Clinical Pharmacology, Safety and Efficacy and Biopharmaceutic Studies specific to colesevelam hydrochloride are provided by cross reference to the approved NDAs for capsule and tablet formulations of Welchol™, NDA 21-141 and NDA 21-176, respectively. This module contains an [in-vitro Bioequivalence \(BE\) Study](#) that demonstrate the *in-vitro* BE between the currently marketed tablets and the powder dosage form.

### **Documents that will be provided after NDA submission**

As agreed upon in the pre-NDA teleconference discussion with FDA and reflected in FDA minutes dated March 19, 2008, three (3) month stability data for two production batches of Welchol™ (b) (4) for Oral Suspension will be submitted as an amendment to the pending NDA by month 5 of the review cycle.

### **Regulatory History and Agreements**

The development program for Welchol™ (b) (4) for Oral Suspension was initiated with the filing of a development plan to NDA 21-176 on January 16, 2004. Subsequently, multiple submissions were made, and a pre-NDA meeting teleconference (TC) was held with FDA to discuss the development of the powder dosage form. Hyperlinks to Sponsor correspondence, FDA communications and Sponsor and FDA meeting minutes are provided in [Module 1.6.3](#). The below table provides a chronological summary outlining the key documentation associated with this NDA.

<b>Date</b>	<b>Topic</b>
January 16, 2004	<a href="#">1. Welchol™ (b) (4) Clinical Development Plan (CDP)</a>
August 30, 2004	<a href="#">2. FDA response to CDP questions</a>
January 18, 2008	<a href="#">3. FDA letter requiring updated EA information in future applications</a>
March 7, 2008	<a href="#">4. EA revision and update proposal</a>
March 19, 2008	<a href="#">5. FDA pre-NDA meeting minutes (March 13 TC)</a>
March 25, 2008	<a href="#">6. Sponsor pre-NDA meeting minutes (March 13 TC)</a>
April 10, 2008	<a href="#">7. FDA response to EA proposal with recommendations</a>
April 29, 2008	<a href="#">8. EA recommendation clarification</a>
May 27, 2008	<a href="#">9. FDA response to EA clarification request</a>

## Summary of Key Agreements

Key agreements reached at meetings and in correspondence are summarized below. This summary is not intended to capture all agreements; therefore, hyperlinks to copies of these documents are provided in the table above and [Module 1.6.3](#).

### FDA Responses to Clinical Development Plan (CDP) on August 30, 2004

- € FDA agreed that demonstration of *in-vitro* BE of the powder formulation (as described in the CDP submitted January 16, 2004) should be adequate for approval for the dosage form.
- € FDA agreed that bile acid binding assays described in the CDP should be adequate to demonstrate bioequivalence between the marketed tablet and proposed powder formulation.
- € A complete NDA drug product package was recommended by FDA
- € FDA recommended the dosage form nomenclature is “colesevelam HCl (b) (4) for oral suspension”

### FDA Approval Letter to NDA 21-176/S-017 on January 18, 2008

- € FDA requested an updated and revised Environmental Assessment (EA) for future applications.

### Pre-NDA meeting teleconference on March 13, 2008

During this teleconference, FDA made the following agreements to support the registration of Welchol™ (b) (4) for Oral Suspension.

- € FDA agreed to the proposal to cross reference elements of drug substance CMC and to cross reference all nonclinical, clinical and clinical pharmacology from the approved Welchol™ NDAs 21-141 and 21-176.
- € FDA agreed to the Sponsor incorporating the powder dosage form information into the existing approved package insert to have a single labeling common to the oral drug products.
- € FDA agreed that a risk management plan is not required for filing of the NDA.

€ Based on the CPSC petition outcome decision, FDA agreed to the proposal to discontinue the stability study of a packaging configuration that will not be part of the commercial product.

€ FDA agreed to the Sponsor's proposal to submit a CBE-30 supplement for the extension of the product's expiry period based on full long term data of the registration batches.

€ FDA agreed to the Sponsor's approach utilizing *in-vitro* binding assay of the bile salts for demonstrating BE.

€ FDA agreed to the amendment of the pending NDA with 3 months of stability data for two demonstration batches by month 5 of the review cycle without extension of the review clock.

**FDA response to updated EA proposal on April 10, 2008**

FDA recommended additional data to address potential terrestrial risks and revised estimates of environmental concentrations.

**FDA response to revised EA clarification on May 27, 2008.**

FDA agreed to the Sponsor's approach for estimating aquatic concentrations of the drug substance with exposure to the terrestrial environment.



Daiichi-Sankyo

DAIICHI SANKYO PHARMA DEVELOPMENT

a Division of DAIICHI SANKYO, INC.

399 Thornall Street, Edison, NJ 08837

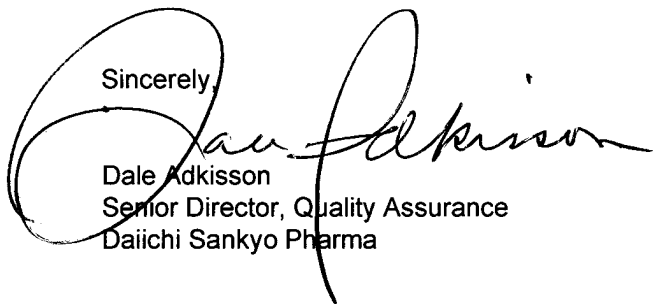
Tel 732 590 5000

July 21, 2008

This letter certifies that the facilities, equipment, methods, procedures and records employed by Daiichi Sankyo Pharma in the testing and manufacturing of finished pharmaceutical products are in compliance with Current Good Manufacturing Practices as outlined in 21CFR§210 & 21CFR§211.

Daiichi Sankyo Pharma, Edison New Jersey is a registered FDA facility. Our facility registration number is 3003089536. Our last FDA inspection was February 89 & 15, 2007. No inspectional observations were issued.

Sincerely,



Dale Addisson  
Senior Director, Quality Assurance  
Daiichi Sankyo Pharma



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-176

Daiichi-Sankyo, Inc.  
Attention: Paulette Kosmoski  
Executive Director, US/EU & Regional Regulatory Affairs-CMC  
399 Thornall Street  
Edison, NJ 08837

Dear Ms. Kosmoski:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Welchol (colesevelam HCl) Tablets.

We also refer to the teleconference between representatives of your firm and the FDA on March 13, 2008. The purpose of the teleconference was to provide some clarification for specific responses sent to you regarding the development of a (b) (4) for Oral Suspension. Preliminary responses to the questions contained in your February 11, 2008 background package were forwarded to you on Monday, March 10, 2008, and you requested a teleconference, in lieu of a face-to-face meeting, to provide some clarification to three of the issues.

The preliminary responses along with the clarification provided at the March 13 teleconference meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at 301-796-1234.

Sincerely,

*{See appended electronic signature page}*

Kati Johnson  
Project Manager  
Division of Metabolism and Endocrinology Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Enclosure



## MEMORANDUM OF TELECONFERENCE MINUTES

**DATE:** March 13, 2008  
**TIME:** 11 am  
**APPLICATION:** NDA 21-176  
**DRUG NAME:** Welchol (colesevelam HCl) Tablets  
**TYPE OF MEETING:** Initially scheduled as a pre-supplement meeting  
**MEETING CHAIR:** Eric Colman, MD  
**MEETING RECORDER:** Kati Johnson  
**FDA ATTENDEES:**

Division of Metabolism and Endocrinology Products  
Eric Colman, MD-Deputy Director, Lipid Team Leader  
Eileen Craig, MD-Clinical Reviewer  
Kati Johnson-Project Manager

Office of Translational Sciences, Office of Clinical Pharmacology  
Sally Choe, PhD-Team Leader  
Sang Chung, PhD-Clinical Pharmacology Reviewer

Office of New Drug Chemistry, Division of Pre-Marketing Assessment I  
Su Tran, PhD-Product Assessment Lead

### EXTERNAL CONSTITUENT ATTENDEES:

Lisbeth Hume, PhD, Executive Director, Pharmaceutical Development  
Paulette Kosmoski, Executive Director, Regulatory Affairs-CMC  
Sandra Smith, RPh, MBA, Senior Director, Regulatory Affairs  
Daniel Brois, PhD, Director, Project Management  
Zoya Borodanski, Associate Director, Regulatory Affairs-CMC  
Gretchen Golikov, Associate Director, Regulatory Affairs  
Jack Rosen, Associate Director, CMC Management & Operations

### BACKGROUND:

Welchol was approved on May 26, 2000 as both tablet (NDA 21-176) and capsule (NDA 21-141) formulations; the latter has never been marketed. It is a bile acid sequestrant indicated: -as an adjunct to diet and exercise to reduce elevated LDL-C in patients with primary hyperlipidemia as monotherapy or in combination with a statin, and to -to improve glycemic control in adults with type 2 diabetes mellitus.

The firm requested a pre-NDA meeting to discuss their plans for submission of a new NDA for a powder for oral suspension formulation. Preliminary responses to the firm's questions were sent to them on March 10, 2008. The firm wanted to provide some feedback on 3 of the responses we sent them, so a teleconference was held in lieu of the previous scheduled face-to-face meeting.

### DISCUSSION POINTS:

The following preliminary responses were forwarded to the firm. The firm's questions are in regular text, our preliminary responses are **bolded**, and any teleconference discussion is in *italics*.

1. We intend to cross reference drug substance CMC and all nonclinical, clinical and clinical pharmacology from the approved Welchol NDAs (21-141/21-176) with subsequent related supplements and Annual Report information. Does the Agency agree that this is sufficient for the CTD filing?

**FDA Preliminary Response: Yes. With regard to CMC, include the following information on the drug substance in the new NDA: A brief section on the general properties of the drug substance, current regulatory specifications of the drug substance, a list of all current manufacturing and testing facilities with a readiness statement for FDA's GMP inspections, and a reference to the complete Chemistry, Manufacturing, and Controls documentation in the approved NDAs.**

*Teleconference Discussion: None*

2. We intend to expand the approved Welchol package insert to appropriately incorporate the powder dosage form. Is this approach to have a single labeling common to the oral drug products acceptable to the Agency?

**FDA Preliminary Response: Yes**

*Teleconference Discussion: None*

3. We plan to have pediatric data for the tablet dosage form submitted to the Welchol NDA 21-176. Consequently, we intend to request a waiver for the need for evaluation of this dosage form in the pediatric population. Does the Agency confirm this position?

**FDA Preliminary Response: Yes**

*Teleconference Discussion: None Teleconference Discussion: None*

4. Based on the well established safety profile of the drug substance from NDA 21-176, no risk minimization actions are planned. A standard pharmacovigilance approach will be used in monitoring adverse drug reactions for the marketed product. Based on this information, we believe that a risk management plan is not required for the CTD. Does the Agency agree?

**FDA Preliminary Response: Yes**

*Post-Teleconference Note: A risk management plan is not required for filing of the NDA. Whether one is necessary for approval is a review issue.*

5. In support of the original NDAs (21-141/21-176), an Environmental Assessment (EA) was filed on July 30, 1999 in accordance with the July 1998 FDA Guidance for Industry: Environmental Assessment of Human Drug and Biologic Applications." The Welchol (b) (4) NDA will cross reference the prior EA section as accompanying primary information. The new Environmental Assessment information to be provided in the Welchol (b) (4) NDA will be the updated expected introduction concentration (EIC) calculated based on anticipated increased use in connection with this dosage form. Do you agree with this approach?

**FDA Preliminary Response: This will be addressed in writing under separate cover.**

*Teleconference Discussion: None*

6. A petition is filed to the CPSC to request an exemption be granted for special packaging requirements for the drug product. In the interim, the registration stability study monitors drug product packaged in both (b) (4). Based on when the CPSC decision is received we plan to discontinue monitoring of one of the packaging systems in the ongoing real time stability study. However, the duration of the stability monitoring will continue to the time point of the FDA assigned expiry period has been reached for the involved packaging system. Is this acceptable to the Agency?

**FDA Preliminary Response: Yes, we agree with your proposal to discontinue the stability study of the packaging configuration that will not be part of the commercial product, and that an amendment submitted during the NDA review cycle for this specific stability protocol modification will not extend the review clock.**

*Teleconference Discussion: None*

7. As the registration batch size is identical to the planned commercial batch size, we propose the extension of the drug product expiry date be based on the registration batches real time stability data. Does the Agency agree with this approach?

**FDA's Response: Yes, we agree with your proposal to submit a CBE-30 supplement for the expiration period extension based on full long-term data of the registration batches.**

*Teleconference Discussion: None*

8. The approach to demonstrate bioequivalence between the tablet and powder dosage forms will utilize *in vitro* binding assays of bile salts. The powder analysis samples are taken from the 2.5 g fill size pouch for the equilibrium study and from the 5 g fill size pouch for the kinetics study. Is this acceptable to the Agency?

**FDA Preliminary Response: Yes, your approach utilizing *in vitro* binding assay of bile salts is acceptable for demonstrating bioequivalence. Provide, in the NDA, why you are using different fill size pouch samples for each study (i.e., equilibrium study vs. kinetics study).**

*Teleconference Discussion: The firm said there was an error in the meeting background package. Both the equilibrium study and the kinetics study used the same size (5.0 grams) pouch. Therefore, the explanation requested above for why different fill size pouch samples were used is not longer necessary.*

9. The registration batches were produced in (b) (4) site facility and the intended commercial production site is the firm's (b) (4) site facility. Batches of drug product made at the (b) (4) location used equipment, processes, procedures the same as or equivalent to the (b) (4) facility. We wish to confirm the approach to providing information/data content in the application to represent the (b) (4) location is acceptable to the Agency.

**FDA Preliminary Response: Yes, we agree with your proposal to submit in the initial NDA submission 12 months of long-term stability data and 6 months of accelerated data for the six registration batches and to amend the NDA with 3 months of stability data for the two production batches, provided that you submit this specific amendment prior to month 5 of the review cycle in order to prevent an extension of the review clock.**

*Teleconference Discussion: The sponsor confirmed that any stability data will be submitted by month 5 of the review cycle. They will notify the Agency prior to submission.*

10. There are 2 fill size package presentations for the powder drug product. Specifically, the 2.5 g pouch contains the dose equivalence to 3 Welchol tablets 625 mg and correspondingly the 5 g pouch contains the dose equivalence to 6 Welchol tablets. The batch size of the registration batches manufactured under production conditions is (b) (4) which is the planned commercial scale in the application. Therefore, we believe the requirement to manufacture (b) (4) of the largest lot planned for full production or a minimum of (b) (4) has been satisfied by the fact that the registration batches and planned commercial batch sizes are identical. Does the Agency concur?

**FDA Preliminary Response:** Our comment in the 30-AUG-2004 letter "... the test batch or lot of the sachet formulation must be manufactured under production condition and must be of a size at least (b) (4) of the largest lot planned for full production or a minimum of (b) (4) whichever is larger" refers to the batch(es) used in the in vitro bioequivalence study. If one or more of your registration batches was used in this study, then our requirement has been met.

**Additional comment:** We note your comments on page 48 of the briefing package regarding the planned change in production scale, from the current (b) (4) (to (b) (4) to the future (b) (4). We agree with your proposal to amend the NDA with 3 months of stability data for the (b) (4) provided that the data will be for at least one batch of each dosage strength (or fill size) and that you submit this specific amendment prior to Month 5 of the review cycle in order to prevent an extension of the review clock.

*Teleconference Discussion:* The firm clarified that the (b) (4) to be packaged will be in addition to the (b) (4) to be packaged, and they intend to submit information on both the (b) (4) and the (b) (4) within the timeframe requested by the Agency.

11. Is the approach of providing a copy of a single executed batch record for each pouch fill size (i.e., 2.5 g and 5 g) of drug product acceptable to the Agency?

**FDA Preliminary Response:** Yes, we agree that a copy of the executed batch record(s) for one batch of each dosage strength (or fill size) will be adequate, provided that the batches were used in the primary stability study or in the bioequivalence study as per 21 CFR 314.50(d)(1)(ii)(b).

**Additional general comment:** We note that your proposed drug product specifications are similar to those of Welchol Tablets, with modifications only for the physical and compositional differences. We recommend that you add testing for attributes specifically relevant to the new dosage form, such as pH for the reconstituted suspension, particle size distribution, redispersibility or suspendability, viscosity, etc., or provide a justification for the lack of such testing. In addition, provide in the NDA a discussion on product-specific degradants because your proposed specification for the powder product has the same identified impurities/degradants found in the tablets.

*Teleconference Discussion:* None

#### **DECISIONS (AGREEMENTS) REACHED:**

None

#### **UNRESOLVED ISSUES OR ISSUES REQUIRING FURTHER DISCUSSION:**

The firm's question (#5) regarding their plans to update their Environment Assessment (EA) from that provided for the initial NDA submission will be addressed in writing under separate cover.

**ACTION ITEMS:**

The Agency will respond to the EA question, as to whether their proposal is acceptable, in a separate written correspondence.

**ATTACHMENTS/HANDOUTS:**

The firm provided an update to the FDA preliminary responses, and they are attached.

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/s/

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Kati Johnson  
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