PERMIT TO CONSTRUCT

Under the authority of RSMo 643 and the Federal Clean Air Act the applicant is authorized to construct the air contaminant source(s) described below, in accordance with the laws, rules and conditions as set forth herein.

Permit Number: 122009-011  Project Number: 2009-07-020

Parent Company: Teva Pharmaceuticals USA
Parent Company Address: 650 Cathill Road, Sellersville, PA 18960
Installation Name: Teva Pharmaceuticals USA
Installation Address: 5000 Snyder Drive, Mexico, MO 65265
Location Information: Audrain County, S4, T50N, R8W

Application for Authority to Construct was made for:
Increase in the allowed annual number of Amoxicillin batches from 1,250 batches per year to 2,100 batches per year. This review was conducted in accordance with Section (5), Missouri State Rule 10 CSR 10-6.060, Construction Permits Required.

☐ Standard Conditions (on reverse) are applicable to this permit.
☐ Standard Conditions (on reverse) and Special Conditions are applicable to this permit.

DECEMBER 17, 2009
DIRECTOR OR DESIGNEE
DEPARTMENT OF NATURAL RESOURCES
STANDARD CONDITIONS:

Permission to construct may be revoked if you fail to begin construction or modification within two years from the effective date of this permit. Permittee should notify the Air Pollution Control Program if construction or modification is not started within two years after the effective date of this permit, or if construction or modification is suspended for one year or more.

You will be in violation of 10 CSR 10-6.060 if you fail to adhere to the specifications and conditions listed in your application, this permit and the project review. In the event that there is a discrepancy between the permit application and this permit, the conditions of this permit shall take precedence. Specifically, all air contaminant control devises shall be operated and maintained as specified in the application, associated plans and specifications.

You must notify the departments’ Air Pollution Control Program of the anticipated date of start up of this (these) air contaminant sources(s). The information must be made available not more than 60 days but at least 30 days in advance of this date. Also, you must notify the Department of Natural Resources Regional office responsible for the area within which you are located within 15 days after the actual start up of this (these) air contaminant source(s).

A copy of this permit and permit review shall be kept at the installation address and shall be made available to Department of Natural Resources’ personnel upon request.

You may appeal this permit or any of the listed special conditions to the Administrative Hearing Commission (AHC), P.O. Box 1557, Jefferson City, MO 65102, as provided in RSMo 643.075.6 and 621.250.3. If you choose to appeal, you must file a petition with the AHC within 30 days after the date this decision was mailed or the date it was delivered, whichever date was earlier. If any such petition is sent by registered mail or certified mail, it will be deemed filed on the date it is mailed. If it is sent by any method other than registered mail or certified mail, it will be deemed filed on the date it is received by the AHC.

If you choose not to appeal, this certificate, the project review and your application and associated correspondence constitutes your permit to construct. The permit allows you to construct and operate your air contaminant sources(s), but in no way relieves you of your obligation to comply with all applicable provisions of the Missouri Air Conservation Law, regulations of the Missouri Department of Natural Resources and other applicable federal, state and local laws and ordinances.

The Air Pollution Control Program invites your questions regarding this air pollution permit. Please contact the Construction Permit Unit at (573) 751-4817. If you prefer to write, please address your correspondence to the Missouri Department of Natural Resources, Air Pollution Control Program, P.O. Box 176, Jefferson City, MO 65102-0176, attention: Construction Permit Unit.
REVIEW OF APPLICATION FOR AUTHORITY TO CONSTRUCT AND OPERATE
SECTION (5) REVIEW

Project Number: 2009-07-020
Installation ID Number: 007-0040
Permit Number: 

Teva Pharmaceuticals USA
5000 Snyder Drive
Mexico, MO 65265

Parent Company:
Teva Pharmaceuticals USA
650 Cathill Road
Sellersville, PA 18960

Audrain County, S4, T50N, R8W

REVIEW SUMMARY

- Teva Pharmaceuticals USA has applied for authority to increase the allowed annual number of Amoxicillan batches from 1,250 batches per year to 2,100 batches per year.

- Hazardous Air Pollutant (HAP) emissions are expected from the proposed equipment. The main HAP of concern from this process is methylene chloride. Other HAPs include triethylamine.

- Subpart Kb of the New Source Performance Standards (NSPS), Standards of Performance for Volatile Organic Liquid Storage Vessels (Including Petroleum Liquid Storage Vessels) for Which Construction, Reconstruction, or Modification Commenced after July 23, 1984, applies to storage tanks identified as T-008 and T-010.


- A carbon adsorption unit (APC-18) is being used to control the methylene chloride emissions from the equipment used to make amoxicillin. Special conditions pertaining to the carbon adsorption unit can be found in Permit No. 092002-004.

- This review was conducted in accordance with Section (5) of Missouri State Rule 10 CSR 10-6.060, Construction Permits Required. Potential emissions of all pollutants are below de minimis levels.
• This installation is located in Audrain County, an attainment area for all criteria air pollutants.

• This installation is on the List of Named Installations [10 CSR 10-6.020(3)(B), Table 2, Item 20 “Chemical Process Plant].

• Ambient air quality modeling was not performed since potential emissions of the application are below de minimis levels

• Emissions testing is not required for the equipment.

• A revision to your Part 70 Operating Permit application is required for this installation within 1 year of equipment startup.

• Approval of this permit is recommended without special conditions.

INSTALLATION DESCRIPTION

TEVA Pharmaceutical USA (Teva) produces several pharmaceutical products (bulk antibiotic preparations) and intermediates (needed to manufacture the final antibiotic products) at its plant in Mexico, Missouri. Teva uses a variety of chemicals including solvents classified as volatile organic compounds (VOCs) and HAPs in a number of pharmaceutical manufacturing processes to produce its final and intermediate products. These processes typically consist of chemical synthesis steps, followed by product separation and drying. The installation was initially constructed in 1989. The existing installation is a major source of VOC emissions. A Part 70 Operating Permit (OP2008-021) was issued in April of 2008. The Operating Permit is currently under review for an administrative amendment.

The following permits have been issued to Teva Pharmaceuticals USA from the Air Pollution Control Program.

Table1: Previously Issued Construction Permits

<table>
<thead>
<tr>
<th>Permit Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0989-004</td>
<td>Construction of a pharmaceutical production facility</td>
</tr>
<tr>
<td>1292-012</td>
<td>Increase Dane salt production and alter boiler operation</td>
</tr>
<tr>
<td>0395-002</td>
<td>Install solvent recovery (distillation) systems, operational changes</td>
</tr>
<tr>
<td>0797-032</td>
<td>Cephalosporin G expansion (2 reactors, 2 receivers, 2 holding tanks)</td>
</tr>
<tr>
<td>0597-013</td>
<td>Install two new dual fuel boilers</td>
</tr>
<tr>
<td>0198-024</td>
<td>Install bis-trimethylsilylurea manufacturing process</td>
</tr>
<tr>
<td>0198-034</td>
<td>Install amoxicillin trihydrate manufacturing process</td>
</tr>
<tr>
<td>1298-010</td>
<td>Install Cefaclor manufacturing process within existing equipment</td>
</tr>
<tr>
<td>0399-010</td>
<td>Install Cephalexin recovery equipment</td>
</tr>
<tr>
<td>102001-011</td>
<td>Modification of the Cephalexin process to increase production</td>
</tr>
<tr>
<td>092002-014</td>
<td>Modification to the existing Amoxicillin manufacturing process for increased production</td>
</tr>
<tr>
<td>022003-014</td>
<td>Modification to existing equipment to recover Cephalexin Monohydrate USP (Bulk) from the mother liquors (ML)</td>
</tr>
<tr>
<td>082003-002</td>
<td>Installation of a regenerative thermal oxidizer</td>
</tr>
</tbody>
</table>
PROJECT DESCRIPTION

TEVA Pharmaceuticals USA (Teva) has applied for authority to modify the existing Amoxicillin manufacturing process to allow for increased production from 1,250 batches per year to 2,100 batches per year. The Amoxicillin process was permitted for 1,500 batches per year in Permit No. 092002-014. In Project No. 2006-05-048, changes in the method used to produce Amoxicillin decreased the annual number of batches to 1,250, but increased the batch size from 490 kilograms to 588 kilograms. Teva is now proposing to increase production by decreasing the lag time between finishing a batch and starting the subsequent one within the initial set of reactors operated in the Amoxicillin pharmaceutical manufacturing process unit (PMPU). The requested increase in Amoxicillin production does not involve any additional process equipment or physical modifications of the existing equipment.

EMISSIONS/CONTROLS EVALUATION

The emission factors and control efficiencies used in this analysis were based on revised calculations submitted by Teva on September 29, 2009. A mass balance approach was used based on a maximum production rate of 2,100 batches per year. The carbon adsorption unit used to control the emissions from this process has a control efficiency of 95%. Special conditions for the control device can be found in Permit No. 092002-014. (Note that even though methylene chloride is considered a HAP, it is not considered a VOC.)

Potential emissions of the application are based on the production of 2,100 batches which is the maximum amount of batches that can be produced while operating continuously (8760 hours per year). Existing potential emissions were obtained from the previous permit (Permit No. 082003-002). Existing actual emissions were obtained from the Teva’s 2008 Emission Inventory Questionnaire (EIQ) submittal. The following table provides an emissions summary for this project.

Table 2: Emissions Summary (tons per year)

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>PM$_{10}$</td>
<td>15.0</td>
<td>&gt;100</td>
<td>0.33</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>SOx</td>
<td>40.0</td>
<td>&gt;100</td>
<td>0.02</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>NOx</td>
<td>40.0</td>
<td>&gt;100</td>
<td>4.06</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>VOC</td>
<td>40.0</td>
<td>&gt;100</td>
<td>23.7</td>
<td>0.91</td>
<td>N/A</td>
</tr>
<tr>
<td>CO</td>
<td>100.0</td>
<td>&gt;100</td>
<td>0.51</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>HAPs</td>
<td>10.0/25.0</td>
<td>N/D*</td>
<td>8.46</td>
<td>10.24</td>
<td>N/A</td>
</tr>
<tr>
<td>Methylene chloride</td>
<td>10.0</td>
<td>N/D</td>
<td>4.52</td>
<td>9.32</td>
<td>N/A</td>
</tr>
<tr>
<td>Methanol</td>
<td>10.0</td>
<td>N/D</td>
<td>2.43</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Toluene</td>
<td>10.0</td>
<td>N/D</td>
<td>1.07</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Triethylamine</td>
<td>10.0</td>
<td>N/D</td>
<td>0.31</td>
<td>0.91</td>
<td>N/A</td>
</tr>
</tbody>
</table>

N/A = Not Applicable; N/D = Not Determined
*The existing total and individual HAPs were not calculated for the installation. Teva is already subject to a MACT and are required to submit a Part 70 due to their major source status for other pollutants.
PERMIT RULE APPLICABILITY

This review was conducted in accordance with Section (5) of Missouri State Rule 10 CSR 10-6.060, Construction Permits Required. Potential emissions of all pollutants are below de minimis levels.

APPLICABLE REQUIREMENTS

Teva Pharmaceuticals USA shall comply with the following applicable requirements. The Missouri Air Conservation Laws and Regulations should be consulted for specific record keeping, monitoring, and reporting requirements. Compliance with these emission standards, based on information submitted in the application, has been verified at the time this application was approved. For a complete list of applicable requirements for your installation, please consult your operating permit.

GENERAL REQUIREMENTS

- **Submission of Emission Data, Emission Fees and Process Information**, 10 CSR 10-6.110
  The emission fee is the amount established by the Missouri Air Conservation Commission annually under Missouri Air Law 643.079(1). Submission of an Emissions Inventory Questionnaire (EIQ) is required June 1 for the previous year's emissions.

- **Operating Permits**, 10 CSR 10-6.065

- **Restriction of Particulate Matter to the Ambient Air Beyond the Premises of Origin**, 10 CSR 10-6.170

- **Restriction of Emission of Visible Air Contaminants**, 10 CSR 10-6.220

- **Restriction of Emission of Odors**, 10 CSR 10-3.090

SPECIFIC REQUIREMENTS


- **Maximum Achievable Control Technology (MACT) Regulations**, 10 CSR 10-6.075, National Emission Standards for Pharmaceutical Production, 40 CFR Part 63, Subpart GGG

**STAFF RECOMMENDATION**

On the basis of this review conducted in accordance with Section (5), Missouri State Rule 10 CSR 10-6.060, *Construction Permits Required*, I recommend this permit be granted without special conditions.

____________________________
Susan Heckenkamp
Environmental Engineer

PERMIT DOCUMENTS

The following documents are incorporated by reference into this permit:

• The Application for Authority to Construct form, dated July 8, 2009, received July 9, 2009, designating Teva Pharmaceuticals USA as the owner and operator of the installation.

• Corrections to the Application for Authority to Construct received via email, dated September 29, 2009.

• Northeast Regional Office Site Survey, dated August 13, 2009.
Mr. Don Reichert  
Teva Pharmaceuticals USA  
5000 Snyder Drive  
Mexico, MO  65265  


Dear Mr. Reichert:  

Enclosed with this letter is your permit to construct. Please study it carefully. Also, note the special conditions, if any, on the accompanying pages. The document entitled, "Review of Application for Authority to Construct," is part of the permit and should be kept with this permit in your files.  

Operation in accordance with these conditions, your new source review permit application and with your revised operating permit is necessary for continued compliance.  

The reverse side of your permit certificate has important information concerning standard permit conditions and your rights and obligations under the laws and regulations of the State of Missouri.  

If you have any questions regarding this permit, please do not hesitate to contact Susan Heckenkamp, at the Departments’ Air Pollution Control Program, P.O. Box 176, Jefferson City, MO  65102 or at (573) 751-4817. Thank you for your attention to this matter.  

Sincerely,  

AIR POLLUTION CONTROL PROGRAM  

Kendall B. Hale  
New Source Review Unit Chief  

KBH:shl  

Enclosures  

c: Northeast Regional Office  
PAMS File: 2009-07-020  

  Permit Number: