CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204031Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

M E M O R A N D U M

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

DATE: 10 June 2013

TO: NDA 204031

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cc: Dominic Chiapperino
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SUBJECT: Product Quality Microbiology assessment of Microbial Limits for Xartemis [Submission Date: 24 May 2013]

The NDA for Xartemis does not include a Microbial Limits release specification for drug product release or stability; however, the applicant provides a suitable rationale for the exclusion of this testing. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.

The proposed drug product is a multilayered extended release tablet for oral administration.

The applicant presents a rationale for waiving Microbial Limits testing for product release and stability (module 3.2.P.2.5). The rationale is comprehensive and includes discussion of the manufacturing process, environmental monitoring program, (b) (4) microbiological validation, microbiological testing of critical raw materials, and microbial limits and (b) (4) testing of the three registration batches.

Environmental microbiological monitoring of the manufacturing work surfaces (equipment, counter tops and ancillary equipment) is performed using (b) (4) every other month. Viable air sampling is performed using a (b) (4).

There are (b) (6) steps in the drug product manufacturing process using (b) (6)

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[redacted] Each of the holding times for these [redacted] was validated by testing for Total Aerobic Microbial Count and Total Yeasts and Molds Count according to USP<61> *Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests*. Microbiological testing of these solutions for bioburden was performed at initial time, 12, 24, 36 and 48 hours following solution preparation. The acceptance criteria for these studies were [redacted]. Based on the data (reference to table 1 which is copied from table 3.2.P.2.5-1 of the submission), the applicant proposes holding times of [redacted] for each of these [redacted] holding times.

Table 1. Microbiological Validation of Drug Product [redacted] Holding Times.

[redacted]

The applicant performs microbial limits testing on those raw materials that are predicted to promote microbial growth [redacted]

The applicant performed [redacted] determination on three batches of the drug product at [redacted] different steps in the manufacturing process as shown in table 2 (which is copied from table 3.2.P.2.5-2). The data show that the [redacted] material at each of these [redacted] stages is well below that which allows microbial proliferation [redacted]

[redacted]

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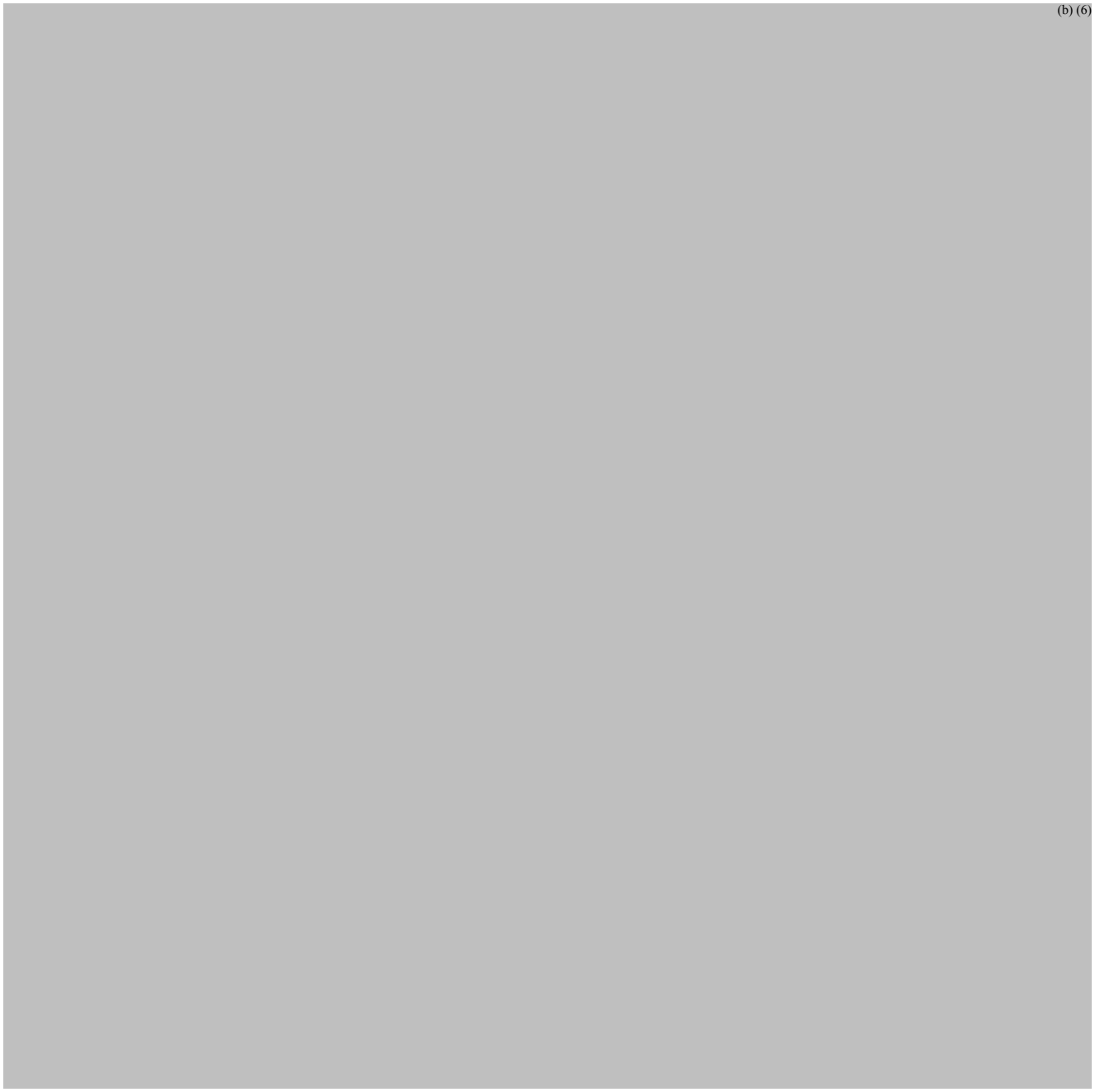

The applicant performed microbial limit testing on the three drug product registration batches. Data are well within limits suggested in USP<1111> and presented in table 4 (copied from table 3.2.P.2.5-3 of the submission).

Table 4. Microbial Limits Testing of Drug Product Registration Batches.

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Sample	Dilution	SCDA (cfu)	TAMC (cfu/g)	SDA (cfu)	TYMC (cfu/g)	E.coli
A82672	1:100	0,0	<100	0,0	<100	Absent
A82673	1:100	0,0	<100	0,0	<100	Absent
A82674	1:100	0,0	<100	0,0	<100	Absent

ADEQUATE

Reviewer Comments – The applicant's proposal to waive microbial limits testing for product release and stability is acceptable.

END

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/s/

JOHN W METCALFE
06/10/2013

STEPHEN E LANGILLE
06/11/2013