DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
8050 Marshall Drive, Suite 205 Lenexa, KS 66214 (913)495-5100 Fax:(913)495-5115	9/9/2019-9/26/2019* FEI NUMBER 3005115360

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Russell D. Odegard, Co-Chief Executive Officer	
FIRM NAME Dynalabs LLC	STREET ADDRESS 2327 Chouteau Ave
CITY, STATE, ZIP CODE, COUNTRY Saint Louis, MO 63103-3010	TYPE ESTABLISHMENT INSPECTED Control Testing Laboratory

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

The accuracy, specificity and reproducibility of test methods have not been established and documented.

Specifically,

The accuracy, specificity, and reproducibility of DYNALABS "core" methods (DLMs) are developed using USP-sourced active pharmaceutical ingredients (APIs) and are not established for individual customer's unique finished dose drug formulations.

Your firm's management stated that all "core" DLMs were validated on USP-sourced API without using a customer-specific finished dose drug formulation in the validation work. This includes:

- Method Validation DLM (b) (4) Lidocaine HCl
- Method Validation DLM (b) (4) Epinephrine
- Method Validation DLM (b) (4) Triamcinolone Acetonide

A) The accuracy and specificity of your "core" DLMs do not assess the customer's formulated API in the presence of expected components such as excipients, degradants, or impurities that may be found in each customer's unique finished dose drug formulation. The lack of accuracy and specificity in "core" DLMs has led your firm to offer procedures such as "(b) (4) ", and (b) (4) to all customers who have not paid for validation extensions, including 503B customers.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Emilie Kahn, Investigator Nicole A Lloyd, Microbiologist Michael G Truchan, Chemist/Biologist X Emilie Kahn Investigator Signed By: 2001100666 Date Signed: 09-26-2019 15:01:08	9/26/2019

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For example, your firm initiated a testing policy allowing customers to submit samples for potency testing on finished dose drug product formulations that "do not have a validation on file." Your firm created a procedure for this policy, summarized in the document CHM 12, *Laboratory Event Investigations*, that states: "For co-elution samples, (b) (4) (b) (4) "

Since February, 2019, use of these "core" DLMs on customer's finished dose drug product samples has resulted in approximately 114 laboratory event investigations (LEIs) for co-elution of peaks, for at least 30 different API-specific "core" DLMs, such as:

Amlodipine DLM (b) (4)
Benzyl Alcohol DLM (b) (4)
Bupivacaine DLM (b) (4)
Bupivacaine HCL DLM (b) (4)
Choline Chloride, DLM (b) (4)
Cyanocobalamin DLM (b) (4)
Dexamethasone Sodium Phosphate DLM (b) (4)
Doxycycline Hyclate DLM (b) (4)
Epinephrine DLM (b) (4)
Estradiol DLM (b) (4)
Estrone DLM (b) (4)
Fentanyl Citrate DLM (b) (4)
Glycopyrrolate DLM (b) (4)
Labetalol DLM (b) (4)
Leuprolide Acetate, DLM (b) (4)
Lidocaine DLM (b) (4)
Methionine, DLM (b) (4)

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Nitroglycerin DLM (b) (4)
Omeprazole, DLM (b) (4)
Oxytocin DLM (b) (4)
Pantoprazole DLM (b) (4)
Phenobarbital DLM (b) (4)
Phenylephrine DLM (b) (4)
Phytonadione, DLM (b) (4)
Prostaglandin DLM (b) (4)
Ropivacaine DLM (b) (4)
Tacrolimus, DLM (b) (4)
Testosterone Cypionate DLM (b) (4)
Testosterone Enanthate DLM (b) (4)
Triamcinolone Acetonide DLM (b) (4)
Triamcinolone Acetonide, DLM (b) (4)
Vancomycin DLM (b) (4)

These LEIs also demonstrate that co-elution issues may remain unresolved despite manipulation of your "(b) (4)." For example, LEI 234 and LEI 238 were opened to investigate co-elution results for an Epinephrine run for (b) (4) %/ (b) (4) %/ (b) (4) (b) (4) # (b) (4), Lot (b) (4). A "(b) (4) (b) (4)" was performed and the co-elution the Epinephrine peak (b) (4). The analyst performed a (b) (4) (b) (4) A passing potency/purity result for Epinephrine, sample W-1-120, using these runs, was released to the client on 5/30/2019.

Finally, document CHM 12, *Laboratory Event Investigations*, also states (b) (4) "

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LEI 72 was opened on 3/6/19 to investigate co-elution in (b) (4) for API Omeprazole using DLM (b) (4) A Chemistry Lead emailed a Technical Services representative to contact the client for approval to "(b) (4) ." A subsequent email states that "Customer has approved…" and (b) (4) for the formulated API, Omeprazole. Passing potency/purity results for Omeprazole, using this run, were released to the client on 3/22/2019.

B) Precision of your "core" DLMs does not include a study of intra-laboratory variation or repeatable results for any customer's unique finished dose drug formulation. Firm management stated that all intermediate precision performed for DLMs used USP-sourced API without using a customer-specific finished dose drug formulation in the validation work.

For example, the following DLMs were validated on USP-grade API without using a customer-specific finished dose drug formulation to perform intermediate precision of these methods:

- Method Validation DLM (b) (4) Lidocaine HCl
- Method Validation DLM (b) (4) Epinephrine
- Method Validation DLM (b) (4) Triamcinolone Acetonide

"Core" DLMs are used to test finished dose drug product samples for 503B customers without validation extensions. At least (b) (4) different 503B customers have submitted samples, for multiple finished dose drug product formulations, and have not received any validation extensions for these formulations.

Your firm could not provide a scientific justification for excluding finished dose drug product formulations from the method validation of your "core" DLMs and your firm could not provide any evidence that these "core"

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DLMs were equivalent to or better than any of the USP methods already available for various finished dose drug formulations that you are testing.

OBSERVATION 2

The written stability program for drug products does not include reliable, meaningful and specific test methods.

Specifically,

DYNALABS method extensions rely on (b) (4) studies performed on USP-grade APIs to support the Certificate of Analysis ("CoA") claim: (b) (4) " However, DYNALABS does not challenge actual finished dose drug product formulations in either the "core" method's (b) (4) study or in the method extension validation study used to support this claim.

For example, in the "core" method validation for DLM (b) (4) Moxifloxacin HCl, (b) (4) preparations of (b) (4) Solution (b) (4) (b) (4) µg/mL Moxifloxacin RS, sourced from USP) were prepared and exposed to various (b) (4) studies which included (b) (4) . In the method extension validation for Moxifloxacin HCl DLM (b) (4) for Sample Lot # (b) (4) one finished drug product sample was prepared and injected (b) (4) on the HPLC and only the %RSD and sample recovery was evaluated. A placebo lot provided by the customer was prepared in duplicate and stored in the customer's container/closure system. One prep was maintained (b) (4) for (b) (4) hours and the other prep was (b) (4) to (b) (4) °C for at least (b) (4) hours. Both were injected into the HPLC and evaluated for the

presences of peaks (b) (4) % of the peak height of the API in the standard injection.

The same testing procedure was used in the following Method Extension Validations, wherein no actual finished dose drug product formulations were challenged:

- Method Extension Validation DLM (b) (4) Lidocaine HCl, Sample Lot # (b) (4)
- Method Extension Validation DLM (b) (4) Lidocaine HCl, Sample Lot # (b) (4) (b) (4), (b) (4)
- Method Extension Validation DLM (b) (4) Epinephrine, Sample Lot # (b) (4)
- Method Extension Validation DLM (b) (4) Triamcinolone Acetonide, Sample Lot# (b) (4)

At least (b) (4) finished dose drug product samples have been run as part of client-indicated time study requests for HPLC potency/purity analysis for 503B customers with method extensions.

OBSERVATION 3

Deviations from written specifications, standards, test procedures and laboratory mechanisms are not recorded and justified.

Specifically,

A) Microbiology analysts do not label plates with initials and correct dates.

For example, plates due for pulling from incubation for reading may have the wrong date. On 9/13/19 and 9/18/19, a micro analyst at your firm was observed not following SOP/MIC 45, specifically:

Plates were pre-labelled "(b) (4) "and "(b) (4) " and "In: Mar 08" and "Out: Mar 13" by an analyst plating dilutions for (b) (4) Testing on 9/13/19. Each plate observed had the incorrect "In:" and "Out:" dates for incubation. MIC 45 procedure step (b) (4) states "(b) (4) ". Furthermore, MIC 45 step (b) (4) tates the analyst is to "(b) (4) ." On 09/18/19, three plates were pre-labeled (1) "(b) (4) and "(b) (4) and "In: 03/14", (2) "(b) (4) " and "In: 03/14" and (3) "(b) (4) " and "In: 03/14." Your firm could not provide a justification for using plates pre-labeled with March dates, for testing that was initiated in September.

B) Your firm could not provide any justification for reporting results as USP compliant, even if only (b) (4) standard injections were used to quantitate a sample due to an injection failing system suitability.

For example, CHM 03.15 Version 11 (effective 1/23/2019), states that (b) (4) ."

Samples W-1-1513 (Lot code (b) (4) and W-1-1515 (Lot code (b) (4)) for BETAMETHASONE SODIUM PHOSPHATE 6MG/ML, received on 1/21/19, were tested for potency/purity using DLM (b) (4) (effective 11/16/2018) on 1/22/19. Only (b) (4) standard injections were used to quantitate the sample results. These results were released to the client on 2/5/2019.

Additionally, instrument (b) (4) Buprenorphine DLM (b) (4) (b) (4) was run for lot (b) (4), and system suitability failed the established specification for percent relative standard deviation (%RSD) due to an injection error with the (b) (4) standard injection. This caused a failed specification that exceeded (b) (4) % RSD. While Deviation D19-370 was initiated to (b) (4) your firm could not provide any justification for calculating (b) (4)

Since February, 2019, at least 120 other laboratory investigations have been initiated for failing RSD due to Injection or Instrument Error.

C) CHM 03.15 Version 11 (effective 1/23/2019), 6.a., 6.b., and 6.c state that the (b) (4) Your firm could not provide any scientific justification for allowing individual analysts to (b) (4) validated methods.

D) HPLC system quality control checks are not measured at suitable intervals to ensure the HPLC analytical systems are within limits for accuracy and precision.

For example, Validation Extension for Moxifloxacin HCl (DLM (b) (4) for Sample Lot # (b) (4) demonstrates an HPLC (b) (4) encompassing (b) (4) injections of prepared drug product samples and placebos. There were no HPLC system quality control checks measured at suitable intervals to ensure that the HPLC analytical system was within limits for accuracy and precision during the approximate (b) (4) hours of sample analysis for these (b) (4) injections. Method extensions using these types of runs have been performed for over (b) (4) customer finished dose drug formulations.

E) Finally, in Deviation D19-440, a primary reference standard used to determine potency for Fentanyl samples was found to be degraded, impacting reported assay results for (b)(4) lots of finished drug product. Your firm relies on internal stability data to establish the expiry of refer ce standards but does not monitor the integrity of standard reference material under normal laboratory use. Three other occurrences of this deviation type were also reported (D19-193, D19-368, and D19-229). However, degradation of reference standards across testing was not investigated and no evaluation was performed to demonstrate that your current procedures for managing reference standards are adequate. These repeated occurrences demonstrate that reference standards may degrade during use, regardless of the expiration date that your firm assigns. Your firm could not provide any justification for failing to ensure the accuracy of potency results when reference standards are degrading with repeated use.

OBSERVATION 4

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically,

The Quality Unit is deficient.

A) Decisions and deviations relating to testing are made without quality unit input, approval, or documentation. Your firm's management stated that laboratory management may communicate with customers through a Technical Services Representative, outside of the Quality unit, to discuss issues with laboratory testing and obtain customer approval for planned deviations, such as (b)(4) or (b)(4) (see **Observation 1**). For example, an email was sent to a customer on 3/22/19 regarding Lot# (b)(4) 1 from a laboratory personnel to Marketing Technical Services stating "(b)(4) ." A Technical Services Representative replied, "Customer has approved the sample. Please result and close out." The Quality Unit was not involved in the communication and your firm's management stated that there is no

documented procedure for this type of communication.

B) Procedures for opening Deviations and initiating CAPAs are not adequate. Deviations are not always opened for systemic issues affecting test results, repeated Occurrences and Deviations are not adequately investigated, and opened investigations do not adequately extend to other lots or methods affected by a discrepancy. The Quality does not investigate deviations in a timely manner and procedures are not always followed.

i. For example, prior to Deviation D19-440 (see **Observation 3**), three other occurrences of this deviation type were reported (D19-193, D19-368, and D19-229). However, no investigation or CAPA was initiated to address these repeated occurrences.

ii. For example, Management of Change Authorization (MOCA) M19-DOC-844, a document change procedure, was initiated to modify the form for document DLM (b) (4) the "core" method for Lidocaine HCl:

"Note: (b) (4) "

No deviation associated with this change to the method was opened and no investigation into previously run lots, potentially impacted by the omission of this note, was performed.

iii. For example, GMP 05 Deviation Investigation and Reporting states that "(b) (4) ."

Approximately 100 Deviations and 120 Occurrences have been opened, and remain open, since January 1, 2019, beyond the (b) (4) deadline to report to the Quality Unit and the (b) (4) deadline for the Quality Unit to close the Deviation or Occurrence.

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