LifePoint Inc.

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WRITTEN COMMENTS REGARDING "GUIDANCE FOR CLINICAL LABORATORY IMPROVEMENT AMENDMENTS OF 1988 (CLIA) CRITERIA FOR WAIVER; DRAFT GUIDANCE FOR INDUSTRY AND FDA"

May 25, 2001

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LifePoint, Inc. (Ontario, Calif.) is a late development stage company currently in the process of commercializing a unique on-site diagnostic test system that will provide "blood-equivalent" results by using saliva (see **Exhibit**). The LifePoint test system uses a special patented flow immunosensor technology, for which the company holds an exclusive worldwide license from the United States Navy Research Laboratories. When used in conjunction with saliva as the test specimen, this unique technology has made it possible for LifePoint to develop a broadly applicable, non-invasive, on-site diagnostic test system that is capable of providing completely automated results for up to10 analytes in under 5 minutes.

The first product LifePoint has elected to develop is the simultaneous detection of the National Institute on Drug Abuse (NIDA) five drugs (marijuana, cocaine, amphetamines/methamphetamine, opiates, and PCP) and alcohol. This menu will quickly be expanded to include other relevant drugs such as prescription drugs including ecstasy, benzodiazepines, barbiturates, and tri-cyclic antidepressants. When applied to substance of abuse testing, the LifePoint product brings the advantages of observable, non-invasive collection, quantitative results that may prove to be evidential for alcohol, and significantly more sensitive and specific results than that which is provided by current immunological urine drug tests (either on-site or lab based). The system, completely automated from collection and processing of the specimen, testing, analysis, result readout and interpretation, eliminates any sample handling and result interpretation. This almost eliminates the chances for operational or interpretive error and potential specimen mix-up, and, therefore, should provide the capability for non-technical personnel to be able to generate the same quality results as a laboratory professional.

All of these benefits can mean significant cost savings and operational improvements for substance of abuse testing in a variety of applications, including emergency room drug overdose cases. Drug testing in these environments is usually conducted by trained professionals, but not necessarily laboratory-trained professionals.

During the past year, LifePoint has presented its technical findings at numerous conferences and seminars. LifePoint has presented at the Drug and Alcohol Testing Industry Association, the International Chiefs of Police Drug Recognition Expert Conference, the Mid-Atlantic Association of Forensic Toxicologists, the Northwest Association of Forensic Toxicologists, the International Association of Forensic Toxicologists, the Society of Forensic Toxicologists, and the American College of Emergency Physicians. LifePoint presented a paper to the International Congress of Alcohol, Drugs and Traffic Safety in Stockholm. Based on the presentations made at the International Congress of Alcohol, Drugs and Traffic Safety, LifePoint was invited to present to the European Union project on roadside drug testing (the ROSITA project). In all instances, LifePoint's presentations were well received. In fact, audiences of employers, law enforcement officials, government representatives, medical professionals,

scientists and researchers have consistently shown a great deal of interest in the flow immunosensor technology and the first product under development by LifePoint.

With such a tremendously positive response to LifePoint's saliva-based, non-invasive, on-site diagnostic test system, we feel it necessary to comment on the recently published " GUIDANCE FOR CLINICAL LABORATORY IMPROVEMENT AMENDMENTS OF 1988 (CLIA) CRITERIA FOR WAIVER; DRAFT GUIDANCE FOR INDUSTRY AND FDA".

Some of the newer products and technologies under development have already addressed many of the concerns raised by this document. It is critical, therefore, for FDA to take into consideration the newer technologies and products that will be shortly available, that can revolutionize on-site diagnostic testing practices, and finally provide the ability to obtain non-invasive, lab-quality results easily, quickly, and cost-effectively on-site by non-technical users.

We recognize and appreciate the effort that the draft represents on the part of FDA. We also appreciate the opportunity to submit these comments and respectfully petition your full consideration of the following:

SALIVA TESTING

Saliva has been extensively validated as a test specimen for a wide variety of analytes, and has been proven to correlate to blood levels for many of these same analytes. Because of this, saliva as a test specimen represents a viable alternative for on-site testing. The use of saliva rather than blood or urine makes it possible to correct a number of burdensome problems that have plagued on-site diagnostics for many years: to be sure, collecting saliva is much less invasive than collecting blood; and, equally important, people find it far less difficult and less offensive providing a saliva sample than providing blood or urine samples.

Interest in the use of saliva for diagnostic testing purposes is growing rapidly and the guideline should not only reflect this, but also be careful not to inadvertently restrict or discourage its use.

CONFORMANCE TO CLIA STATUTE

The CLIA statute, 42 U.S.C. § 263a(d)(3) Examination and Procedures, as modified by FDAMA, reads:

"The examination and procedures...are simple laboratory examinations and procedures that have an insignificant risk of an erroneous result, including those that - (A) employ methodologies that are so simple and accurate as to render the likelihood of erroneous results by the user negligible, **OR** (B) the Secretary has

determined pose no unreasonable risk of harm to the patient if performed incorrectly".

The FDA, in this draft guidance, appears to be changing the original intent of the statute that allows products that are either simple and accurate OR from which there is no reasonable risk of harm from an incorrect result to be exempt, to a requirement that a product meet both requirements before it can be waived. This is not within the original intent of the CLIA statute and should be modified to meet the original intent.

PROFESSIONAL vs. UNTRAINED USERS

The development of simple, easy-to-use on-site testing products should enhance diagnostics and allow for more reliable, accurate, and faster testing methods by untrained users without increasing the cost of such testing. However, the proposed guidelines lean in favor of laboratories in that the proposed test protocols favor professional user test results.

Throughout the proposed guidance, there is a consistent requirement that the results from different untrained users be compared to the same number of results from a single professional user. This study design is biased in favor of the professional user. It has been proven that results from different users can significantly contribute to variation in precision and accuracy (as is evidenced by FDA's own requirement for between-operator precision in this same document). Therefore, the study design should require the same number of professional users performing the same number of tests for comparison. This translates into requiring the same number of professional and untrained users at each site, each performing the same number of tests.

If the intent of these guidelines is to discourage the use of on-site testing by untrained users then this draft guideline will accomplish such a goal. However, if instead the goal of these guidelines is to ensure the overall precision and accuracy, of non-laboratory testing, then the modifications suggested below will ensure that simple products or products that can be used without reasonable risk of harm will receive appropriate validation testing and clearance review.

THE DRAFT GUIDELINE POINT-BY-POINT

The following are recommendations that LifePoint believes should be considered by FDA:

INTRODUCTION

The CLIA statute, 42 U.S.C. § 263a(d)(3) Examination and Procedures, as modified by FDAMA, reads:

"The examination and procedures...are simple laboratory examinations and procedures that have an insignificant risk of an erroneous result, including those that - (A) employ methodologies that are so simple and accurate as to render the likelihood of erroneous results by the user negligible, **OR** (B) the Secretary has determined pose no unreasonable risk of harm to the patient if performed incorrectly".

The draft guidance, in *"Step 2"*, significantly changes the intent of the statute to require not just one, but both (A) **AND** (B) above to be waived. This is a direct contradiction to the intent of the original CLIA statute. The CLIA statute specifically allows a product to be waived if it meets either (A) **OR** (B) and does not require both. In order to be consistent with the legislative statute, Step 2 should be modified as follows:

"Step 2 Determine if the test has an insignificant risk of erroneous result as defined in section **III** of this guidance.

> If FDA determines that the test is simple (step 1) ~~and~~ **or** has an insignificant risk of erroneous result (step 2), and is accurate (step 3),
> THEN it meets the criteria for waiver...."

"***Step 4*** For all tests that are determined to be simple, **or** have an insignificant risk of erroneous result..."

IV. DEMONSTRATING ACCURATE

Untrained/Professional Precision Study for Quantitative Tests

The requirement for 60 untrained users in the study design is unreasonable and burdensome. It is accepted and normal protocol (e.g., NCCLS guidance) to carry out 20-30 determinations for precision/accuracy validations. We therefore recommend the use of 20-30 untrained users divided equally between 3 non-laboratory sites.

Additionally, the requirement that the results from 10 different untrained users be compared to the same number of results from a single professional user is biased in favor of the professional user. It has been proven that results from different users can significantly contribute to variation in precision and accuracy (as is evidenced by FDA's own requirement for between-operator precision in this same document). Therefore, the study design should require the same number of professional users performing the same number of tests for comparison. This translates into requiring the same number of professional and untrained users at each site, each performing the same number of tests.

Similarly, the requirement for different untrained users, but allowing the same professional for the day-to-day variability studies is biased in favor of the professional user. For the reasons outlined above, this requirement should be applied equally to the untrained and professional users – both can remain the same or both should be different every day.

Untrained/Professional Agreement Study for Quantitative Tests

The requirement for 300 untrained users is burdensome and unusual by even FDA standards for Class II diagnostic tests. Tests run by 20-30 untrained users should be sufficient to statistically assess "agreement." The type of statistical analysis required in this section is often done by laboratories to validate their own procedures; their evaluation usually includes one month's test experience – or 20-30 results. Therefore, we strongly recommend that the number of tests required be reduced to 20-30.

As stated in the previous section, the requirement for far fewer professional users versus untrained users to generate the test data is biased in favor of the professional user. The study design should be modified to use the same number of professional and untrained users.

Untrained/Professional Agreement Study for Qualitative Tests

The requirement for testing 300 samples is burdensome and unusual by even FDA standards for Class II diagnostic tests. Since there is a requirement to test at four difference levels, the ability to test 20-30 at each level should be sufficient. Therefore, we recommend the use of a total of 80-120 samples.

As stated above, the requirement for far fewer professional users than untrained users is biased in favor of the professional test data. The number of users should be the same for professional and untrained test results to provide accurate, objective data.

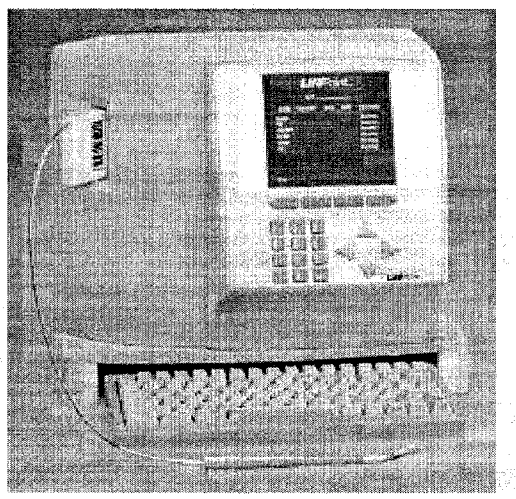
Exhibit

LifePoint, Inc. will soon be introducing a unique product – the first non-invasive, on-site testing system that will deliver blood-equivalent results without taking a blood sample. The system consists of an easy-to-use saliva collection and testing cassette, used in conjunction with a small, portable instrument. It is designed to be user friendly with minimal training required. The first product is designed to quantitatively measure alcohol and screen for the five National Institute on Drug Abuse (NIDA) illicit drugs (marijuana, cocaine, opiates, methamphetamine/ amphetamine and angel dust (PCP) in a single cassette from a few drops of saliva within 5 minutes. The system provides the following advantages:

- **Delivers "blood-equivalent" results**
- **Provides on-the-spot results**
- **Reduces chain-of-custody issues**
- **Minimizes training requirement**
  Eliminates suspect transportation

The small, portable instrument automatically manages all functions related to running the test panel, including:

- **Specimen collection**
- **Sample adequacy and quality checks**
- **Automatic quality control**
- **Sample processing and analysis**
- **Electronic and hard copy test results**
- **Laboratory-quality accuracy and precision performance**
- **Result interpretation**



The test cassette, packaged in a foil pouch, is ready for immediate use and disposal. The saliva specimen, test reagents and waste are contained within the cassette, thereby greatly reducing the possibility of biological contamination.

The entire test procedure, including specimen collection and result printout, takes less than five minutes. Saliva is collected via aspiration, with a device similar to those used in a dental office, and automatically transferred into the test cassette. The collection process itself takes approximately thirty seconds, which is significantly faster than absorbent pad collection (which can take five to fifteen minutes for sample collection alone). Additionally, aspiration allows for quantitative results, which cannot be provided with absorbent pad collection.

Saliva indicates blood-equivalent or "under-the-influence" results, similar to a blood test. Saliva as a test specimen is therefore more relevant than urine for impairment related situations such as post-accident, for suspicion, random, and fit-for-duty tests. Urine as a test specimen indicates drug use over the last 2-5 days. LifePoint's system is the first on-site system to test for drugs of abuse and alcohol simultaneously, and the first on-site test for blood-equivalent "under-the-influence" results. Additionally, the entire process – collection and test – is observable and significantly reduces the possibility of adulteration.

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