To: U.S. Food and Drug Administration Docket No. FDA-2014-N-0233

From: James Harris, Ph.D., Chief Scientific Officer, Vatex Explorations LLC,
Developer of the Divert-X System

http://www.divert-x.com/contact/

Date: 6 June 2014

Subject: The behavioral and economics literature are the genesis of the approach: Vatex leverages established behavioral science to reduce diversion and misuse.

The Notice seeks information on the **effectiveness and acceptability** of interventions that can be applied to reducing the prescription drug crisis. Vatex leverages established behavioral science to reduce diversion and misuse of Controlled Substances.

Divert-X – the dispensing and behavioral monitoring system under development by Vatex – tackles this problem directly by seeking to separate authentic patients from those who are exaggerating the intensity and duration of symptoms. Those who subvert the system to feed an addiction or sell their medications are far less likely to demonstrate the spectrum of dosing behaviors exhibited by compliant, authentic patients. A healthcare insurer has permitted Vatex to pilot Divert-X in a region it serves so that Vatex can demonstrate the efficacy of the intervention via robust science.

The theory of action for our efforts is straightforward and evidence-based: checks & balances for oversight of psychoactive, addictive drugs promote thoughtful use, safer behaviors, and accountability. The Vatex hardware advancements are described in a separate submission to this Docket (search for "Hardware Design") and are used to gather objective data on actual medication-use behaviors. These objective data are currently unavailable for individual patients. The application of proprietary analytics for assessing behavioral markers collected by the packaging is used in a management system designed to reduce diversion and misuse. The management system is termed "Active MTM" and is described in a separate submission to this Docket (search for "Management Systems").

Several behavioral "big data" analogies to the Vatex approach exist. For example, insurers use real-time analytics to remotely uncover dishonest doctors and prevent "pay and chase" schemes (1). Brick-and-mortar and online casinos use real-time analytics to intervene in gambling addiction (2). Efforts of online gambling companies to identify problem gamblers are directly analogous to Divert-X because all data are collected remotely, in real-time, in fine detail, and are related to addiction (2-6). Another analogy is the proprietary credit scoring systems used by the consumer finance industry known as debt-repayment risk algorithms (7-9). The study of hidden human behavior has become central to several subfields of economics and finance (10). Because of this longstanding research focus, the behavioral and economics literature has firmly established that people are more accountable for their actions when they are being scored or merely aware that they might be scored (10-30), but the scoring system must remain somewhat opaque so that it is not subverted. For example, details of banking algorithms (used to score customers and employees) are tightly-held secrets (10). Similarly, the detailed methodology behind medication-use scoring will not be shared with the public generally in order to leverage behavioral science and to protect from subversion.

Vatex sees strong parallels between the human desire to be seen as a good credit risk (rewards include improved loan pricing, employability in high-value positions, lower insurance rates (31-32)) and the desire to be seen as a credible patient (rewards include enhanced trust between provider and patient, straightforward access to needed medications, improved care quality). Bringing trust back to Controlled Substance prescribing and reducing patient-access disparities are key long-term Vatex goals. Employing a sophisticated device as an integral part of dispensing will emphasize to the patient, the family, and caregivers the serious safety risks associated with Controlled Substances. Because many people do not understand the risks of their medications, the packaging itself serves to warn (a behavioral "nudge" (33)) and should result in greater caution being taken to comply with prescribed regimens. Hence, the Divert-X packaging emphasizes safe-use and educational principles.

Precedent from the medical, behavioral, and economics literature show that Divert-X is likely to be a high-impact system. Vatex is combining key refinements of historical systems with its own innovation to address a pressing problem. The medical literature is replete with studies (34-37) showing that compliance to medications not regulated by DEA can be increased through a variety of actions with corresponding improvements in health and cost. Improving compliance to Controlled Substance regimens is much more challenging, however, because overconsumption is spurred by experimentation and addiction, because of the financial windfall for those patients who divert their ongoing prescriptions (38-43), and because current clinical tools cannot separate authentic patients from those exaggerating the intensity and duration of disease (44-49). Hence, the literature describing methods that improve Controlled Substance adherence is sparse. A single European trial has been completed of monitored-access blister cards filled with buprenorphine-naloxone, a drug that is given to opioid addicts (50). The drivers to divert buprenorphine products are strong and multifaceted, and diversion has become so widespread that the outpatient use of buprenorphine is being called into question (51). The trial (50) serves as clear precedent for Divert-X because of strong parallels in form-factor and the focus on Controlled Substances. This small study demonstrated a 39% reduction in treatment costs, principally from reduced clinic visits. The blister cards used in the trial were manufactured by Stora Enso - one of many similar, simple dispensing systems that have been developed. All electronic blister cards engineered to date 1) only monitor time, 2) lack sensing required for behavioral inference and to foil diversionary tactics, and 3) require factory packaging of the medications, so they therefore do not possess the capabilities required to stem the U.S. crisis.

A small survey of opioid addicted criminal offenders who were receiving or soon to receive buprenorphine-based Medication-Assisted Treatment (MAT) was conducted for Vatex. The concept of monitoring individual doses electronically was introduced to each person, along with an illustrative photo. The outcome was that 86% thought that Divert-X monitoring would reduce diversion (24 of 28) while 14% thought that Divert-X would not change diversion. The same question was posed to a group of MAT non-offenders who had become addicted from routine medical care – this group was unanimous in its view that the Divert-X approach is preventive. Regarding the non-offender population "every patient who started using opioids after an accident or injury endorsed the idea that such a device would have saved them from a life of addiction. They believe, pretty unanimously, that such a device would have thwarted that first period of over-use, before the drugs really caught hold of them" (52).

Vatex contends that it is certain that the deployment of Divert-X will reduce misuse and diversion of opiates. Our corporate commercialization strategy is to implement sound science to quantify this impact and to leverage the data to secure adoption among healthcare payers based on their financial self-interest. While Controlled Substances are the initial market for Vatex services, a proven drug-safety system would be utilized in other therapeutic areas.

References

1. Diamond F. Anti-Fraud Efforts Turn to Prevention. Managed Care Magazine Online. September 2013. [cited May 2014]; Available from: http://www.managedcaremag.com/archives/2013/9/anti-fraud-efforts-turn-prevention.

2. Berzon A, Maremont M. Researchers Bet Casino Data Can Identify Gambling Addicts: Computerized models can spot and warn people with high risk profiles similar to the way geneticists have invented tests to predict cancer risk. Wall Street Jounal. August 3, 2013. [cited May 2014]; Available from: http://online.wsj.com/news/articles/SB10001424127887324348504578607903673679448.

3. Braverman J, LaPlante DA, Nelson SE, Shaffer HJ. Using cross-game behavioral markers for early identification of high-risk internet gamblers. Psychology of Addictive Behaviors. 2013;27(3):868-877.

4. Gray HM, LaPlante DA, Shaffer HJ. Behavioral characteristics of Internet gamblers who trigger corporate responsible-gambling interventions. Psychology of Addictive Behaviors. 2012;26(3):527-35.

5. Braverman J, Shaffer HJ. How do gamblers start gambling: identifying behavioral markers for high-risk internet gambling. European Journal of Public Health. 2012;22(2):273-8. PMCID: 3324590.

6. Markham F, Young M, Doran B. Detection of problem gambler subgroups using recursive partitioning. International Journal of Mental Health and Addiction. 2013;11(3):281-291.

7. Brockett PL, Golden LL. Biological and Psychobehavioral Correlates of Risk Taking, Credit Scores, and Automobile Insurance Losses: Toward an Explication of Why Credit Scoring Works. Journal of Risk and Insurance. 2007;74(1):23–63.

8. Smith BC. Stability in Consumer Credit Scores: Level and Direction of FICO Score Drift as a Precursor to Mortgage Default and Prepayment. Journal of Housing Economics. 2011;20(4):285-298. [cited May 2014]; Available from: http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1621755.

9. Bonca BL. Essays on Credit Scores, Strategic Behavior, and Default with Credit Cards. Dissertation, The George Washington University. 2013. [cited May 2014]; Available from: http://gradworks.umi.com/3587867.pdf.

10. Zitzewitz E. Forensic Economics. Journal of Economic Literature 2012;50(3):731-69. [cited May 2014]; Available from: http://www.dartmouth.edu/~ericz/forensic.pdf.

11. Mazar N, Amir O, Ariely D. The Dishonesty of Honest People: A Theory of Self-Concept Maintenance. Journal of Marketing Research. 2008;XLV:633–644. [cited May 2014]; Available from: http://people.duke.edu/~dandan/Papers/PI/Dishonest_JMR.pdf.

12. Pierce L, Snow D, McAfee A. Cleaning House: The Impact of Information Technology Monitoring on Employee Theft and Productivity. Olin Business School, Washington University. August 24, 2013. [cited May 2014]; Available from: http://apps.olin.wustl.edu/faculty/pierce/cleaninghouse.pdf.

13. Nagin D, Rebitzer J, Sanders S, Taylor L. Monitoring, Motivation and Management: The Determinants of Opportunistic Behavior in a Field Experiment. National Bureau of Economic Research, Working Paper 8811, February 2002. [cited May 2014]; Available from: http://www.nber.org/papers/w8811

14. Ljungqvist A, Malloy C, MARSTON F. Rewriting History. The Journal of Finance. 2009;64:1935–1960. [cited May 2014]; Available from: http://finance.wharton.upenn.edu/department/Seminar/2007Spring/micro/ljungqvist-micro032907.pdf.

15. Olken BA. Monitoring Corruption: Evidence from a Field Experiment in Indonesia. Journal of Political Economy. 2007;115(2)200-249. [cited May 2014]; Available from: http://www.povertyactionlab.org/publication/monitoring-corruption-evidence-field-experiment-indonesia.

16. Parsons CA, Sulaeman J, Yates MC, Hamermesh DS. Strike Three: Discrimination, Incentives, and Evaluation. American Economic Review. 2011;101(4):1410-1435. [cited May 2014]; Available from: http://www.nber.org/papers/w13665.

17. Silverman E, Skinner J. Medicare upcoding and hospital ownership. Journal of Health Economics. 2004;23:369–389. [cited May 2014]; Available from: http://www.dartmouth.edu/~jskinner/documents/silvermanskinner.pdf.

18. Simon PA, Leslie P, Run G, Jin GZ, Reporter R, Aguirre A, Fielding JE. Impact of restaurant hygiene grade cards on foodborne-disease hospitalizations in Los Angeles County. Journal of Environmental Health. 2005;67(7):32-36.

19. Slemrod J, Blumenthal M, Christian C. Taxpayer response to an increased probability of audit: evidence from a controlled experiment in Minnesota. Journal of Public Economics. 2001;79:455–483. [cited May 2014]; Available from: http://aysps.gsu.edu/isp/files/ISP_SUMMER_SCHOOL_2008_ERARD_TAXPAYER_RESPONSE.pdf.

20. Pomeranz D. No Taxation without Information: Deterrence and Self-Enforcement in the Value Added Tax. MIT Job Market Paper, January 2010. [cited May 2014]; Available from: http://faculty.chicagobooth.edu/workshops/AppliedEcon/past/pdf/Pomeranz%2009-feb-2011.pdf.

21: Heron RA, Lie E. Does Backdating Explain the Stock Price Pattern Around Executive Stock Option Grants? Journal of Financial Economics. 2007;83(2):271-295. [cited May 2014]; Available from: http://dev3.cepr.org/meets/wkcn/5/5534/papers/Lie.pdf.

22. Jacob BA, Levitt SD. Catching Cheating Teachers: The Results of an Unusual Experiment in Implementing Theory. National Bureau of Economic Research, Working Paper 9414, December 2002. [cited May 2014]; Available from: http://www.nber.org/papers/w9414.pdf?new_window=1.

23. Jin GZ, Leslie P. The Effect of Information on Product Quality: Evidence from Restaurant Hygiene Grade Cards. Quarterly Journal of Economics. 2003;118(2):409-451. [cited May 2014]; Available from: http://kuafu.umd.edu/~ginger/research/restaurant-hygiene-wpversion.pdf.

24. Jin GZ, Leslie P. Reputational Incentives for Restaurant Hygiene. American Economic Journal: Microeconomics. 20091(1):237-67. [cited May 2014]; Available from: http://kuafu.umd.edu/~ginger/research/ReputationAEJFinalVersion.pdf.

25. Kleven HJ, Knudsen MB, Kreiner CT, Pedersen S, Saez E. Unwilling or Unable to Cheat? Evidence from a Randomized Tax Audit Experiment in Denmark. National Bureau of Economic Research, Working Paper 15769, February 2010. [cited May 2014]; Available from: http://www.nber.org/papers/w15769.

26. Christie WG, Harris JH, Schultz PH. Why Did NASDAQ Market Makers Stop Avoiding Odd-Eighth Quotes? Joural of Finance. 1994;49(5):1841-1860. [cited May 2014]; Available from: http://www.acsu.buffalo.edu/~keechung/TEM/Journal%20Articles/Collusion%20B%201994.pdf.

27. Di Tella R, Schargrodsky E. The Role of Wages and Auditing During a Crackdown on Corruption in the City Buenos Aires. Journal of Law and Economics. 2003;46(1):269-292. [cited May 2014]; Available from: http://www.people.hbs.edu/rditella/papers/JLECorrHospital.pdf.

28. Duflo E, Hanna R, Ryan S. Monitoring Works: Getting Teachers to Come to School. CEPR discussion paper DP6682. 2008. [cited May 2014]; Available from: http://courses.cs.washington.edu/courses/cse590f/06au/docs/pal1.pdf.

29. Bateson M, Nettle D, Roberts G. Cues of being watched enhance cooperation in a real-world setting. Biololgy Letters. 2006;2(3):412–414. [cited May 2014]; Available from: http://rsbl.royalsocietypublishing.org/content/2/3/412.full.

30. Nagin DS, Pogarsky G. An Experimental Investigation of Deterrence: Cheating, Self-Serving Bias, and Impulsivity. Criminology. 2003;41(1):167–194.

31. Leamy E. Five Factors That Make Your Credit Score. ABC News, November 29, 2010. [cited May 2014]; Available from: http://abcnews.go.com/Business/credit-score-credit-reports-improve-save-money-elisabeth/story?id=12236208.

32. Kaufman W. Credit Repair Companies Can't Fix Everything. National Public Radio. November 11, 2008. [cited May 2014]; Available from: http://www.npr.org/templates/story/story.php?storyId=96844965.

33. Thaler RH, Sunstein CR. Nudge: Improving Decisions About Health, Wealth, and Happiness. Penguin Books; 2009. ISBN-10: 014311526X.

34. The Center for Connected Health, Partners HealthCare. Wireless Medication Adherence Study Conducted at the Partners Center for Connected Health Shows Promising Initial Findings. June 2010. [cited May 2014]; Available from: http://www.connected-health.org/media-center/press-releases/wireless-medication-adherence-study-conducted-at-the-partners-center-for-connected-health-shows-promising-initial-findings.aspx.

35. Belluck, P. For Forgetful, Cash Helps the Medicine Go Down. The New York Times, June 13, 2010, Health section. [cited May 2014]; Available from: http://www.nytimes.com/2010/06/14/health/14meds.html?pagewanted=all&_r=0.

36. Chang A, Liberman JN, Coulen C, Berger JE, Brennan TA. Value-Based Insurance Design and Antidiabetic Medication Adherence. American Journal of Pharmacy Benefits. 2010;2(1):39-44. [cited May 2014]; Available from: http://www.ajmc.com/publications/ajpb/2010/vol2_no1/Value-Based-Insurance-Design-and-Antidiabetic-Medication-Adherence.

37. Cutrona SL, Choudhry NK, Fischer MA, Servi A, Liberman JN, Brennan TA, Shrank WH. Modes of delivery for interventions to improve cardiovascular medication adherence. American Journal of Managed Care. 2010;16(12):929-942. PMCID: 3115758.

38. Rigg KK, Kurtz SP, Surratt HL. Patterns of prescription medication diversion among drug dealers. Drugs (Abingdon Engl). 2012;19(2):144-155. PMCID: 3365597.

39. United States Court of Appeals, Tenth Circuit. United States of America vs. Martha Earlene Phillips, 2012, Appellate Case 11-6000. [cited May 2014]; Available from: http://www.gpo.gov/fdsys/pkg/USCOURTS-ca10-11-06000/pdf/USCOURTS-ca10-11-06000-0.pdf.

40. Hamacher B. Miami Lakes Man, His Wife and Mother Arrested in $25 Million Prescription Drug Trafficking Scheme: FDLE. NBC 6 South Florida. June 18, 2013. [cited May 2014]; Available from: http://www.nbcmiami.com/news/Miami-Lakes-Man-His-Wife-and-Mother-Arrested-in-25-Million-Prescription-Drug-Trafficking-Scheme-FDLE-212000121.html.

41. Office of Inspector General (OIG), U.S. Department of Health & Human Services. Beneficiary Fraud. The National Consumer Protection Technical Resource Center. [cited May 2014]; Available from: http://www.smpresource.org/Content/NavigationMenu/HealthCareFraud/OIGMedicareFraud/Beneficiary_Fraud.htm.

42. U.S. Government Accountability Office. Medicaid: Fraud and Abuse Related to Controlled Substances Identified in Selected States. GAO-09-957, September, 2009. [cited May 2014]; Available from: http://gao.gov/new.items/d09957.pdf.

43. U.S. Senate Committee on Homeland Security & Governmental Affairs. A Prescription for Waste: Controlled Substance Abuse in Medicaid. Hearing, September 30, 2009. [cited May 2014]; Available from: http://www.hsgac.senate.gov/subcommittees/federal-financial-management/hearings/a-prescription-for-waste-controlled-substance-abuse-in-medicaid.

44. Grover CA, Elder JW, Close RJ, Curry SM. How Frequently are "Classic" Drug-Seeking Behaviors Used by Drug-Seeking Patients in the Emergency Department? Western Journal of Emergency Medicine. 2012;13(5):416-421. PMCID: 3556950.

45. Sansone RA, Sansone LA. Faking attention deficit hyperactivity disorder. Innovations in Clinical Neuroscience. 2011;8(8):10-13. PMCID: 3173757.

46. Davis JF. Professional Drug Seekers Exposed by former Addict. Medical Island. February 20, 2013. [cited May 2014]; Available from: http://www.medicalisland.net/guest-posts/professional-drug-seekers-exposed-by-former-addict.

47. Beck M. Doctors' Challenge: How Real Is That Pain? Even When Patients Describe Pain in Vivid Detail, Doctors Have Few Tools to Determine What's Real. The Wall Street Journal. July 15, 2011. [cited May 2014]; Available from: http://online.wsj.com/news/articles/SB10001424052702304450604576419810283786774.

48. Newton P. How easy is it to fake ADHD? Fake ADHD in just 5 minutes with Google. Psychology Today Online. July 3, 2010. [cited May 2014]; Available from: http://www.psychologytoday.com/blog/mouse-man/201007/how-easy-is-it-fake-adhd.

49. Anonymous. Drug Seekers Suck. Emergency Physicians Monthly. February 4, 2008. [cited May 2014]; Available from: http://www.epmonthly.com/whitecoat/2008/02/drug-seekers-suck/.

50. Tacke U, Uosukainen H, Kananen M, Kontra K, Pentikänen H. A pilot study about the feasibility and cost-effectiveness of electronic compliance monitoring in substitution treatment with buprenorphine-naloxone combination. Journal of Opioid Management. 2009;5(6):321-329.

51. Anson P. Suboxone: The New Drug Epidemic? National Pain Report, American News Report. September 23, 2013. [cited May 2014]; Available from: http://americannewsreport.com/nationalpainreport/suboxone-new-drug-epidemic-8821747.html.

52. Personal communication with Jeffrey Junig MD,PhD, Medical College of Wisconsin and Fond du Lac Psychiatry. October 16, 2013.