To: Washington University IRB

From: Zachary Prensky, CEO - LB Pharmaceuticals

Date: February 15, 2021

RE: Clarification Memo #5

An Open Label Positron Emission Tomography (PET) Study to Evaluate Dopamine Receptor Occupancy of LB-102 Administered Orally to Healthy Subjects

---

The intent of this protocol clarification memo is to provide clarification for the LB-102-002 protocol (11 November 2020, Version 1). All items listed below have been incorporated into the protocol and will be submitted to FDA as a protocol amendment.

Procedures in Case of Emergency – Sponsor Contact Information

Original Wording

Role in Study	*Name*	*Address and Telephone Number*
Chief Medical Officer/Medical Monitor	*Anna Eramo, MD*	*LB Pharmaceuticals, Inc.* *575 Madison Ave., 10th Floor* *New York, NY 10022* *Email: anna@lbpharma.us* *(312)661.2021*
Medical Monitor	*Bruce Reidenberg, MD, FAAP, FCP*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: breidenberg@gmail.com* *Phone: 914-707-4195*
Clinical Project Manager	*Miguel Cabrera, PhD*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: mcabrera@targethealth.com* *Phone: 908-418-8121*
Clinical Project Manager/Safety Monitor	*Luxi Wang, PharmD*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: luwang@targethealth.com* *Phone: 917-660-2597*

Revised Wording

Role in Study	*Name*	*Address and Telephone Number*
Chief Medical Officer/Medical Monitor ***(Secondary Contact)***	*Anna Eramo, MD*	*LB Pharmaceuticals, Inc.* *575 Madison Ave., 10th Floor* *New York, NY 10022* *Email: anna@lbpharma.us* *(312)661.2021*
Medical Monitor ***(Primary Contact)***	*Bruce Reidenberg, MD, FAAP, FCP*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: breidenberg@gmail.com* *Phone: 914-707-4195*
Clinical Project Manager	*Miguel Cabrera, PhD*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: mcabrera@targethealth.com* *Phone: 908-418-8121*
Clinical Project Manager/Safety Monitor	*Luxi Wang, PharmD*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: luwang@targethealth.com* *Phone: 917-660-2597*

Section 1 – Main Criteria for Eligibility: Exclusion Criteria

Original Wording

A subject will be excluded from the study if he or she meets the following criteria:

1. Are pregnant or lactating.

2. Have a history or presence of significant cardiovascular, respiratory, hepatic, renal, gastrointestinal, endocrine, neurological or psychological/psychiatric disorders which, in the opinion of the Investigator, increases the risk of the study drug or may confound the interpretation of study measures.

3. Clinically significant abnormal findings on physical examination or vital signs as determined by PI.

4. Individuals with pacemakers, aneurysm clips, shrapnel, or other restricted implanted metallic devices will be excluded from study. All subjects complete the standard MRI screening questionnaire prior to MRI.

5. History or presence of psychiatric or neurological disease or condition as determined by the PI.

6. History of seizures.

7. Subject with any history or current evidence of suicidal behavior.

8. Unwilling to complete any planned study assessments.

9. Have a history of blood donation in excess of 500 mL of blood within 30 days prior to Screening.

10. Have received treatment with an investigational drug or device within 30 days prior to Screening.

11. Have a positive test for Human Immunodeficiency Virus (HIV) antibodies 1 and 2, Hepatitis B Surface Antigen (HBsAg) or Hepatitis C Virus (HCV) antibody.

12. Any subject who is known to be allergic to the study drug or any components of the study drug.

13. The subject has a fasting blood glucose ≥ 126 mg/dL or hemoglobin A1c (HbA1c) ≥ 6.5% at Screening.

14. The subject has a history of QT prolongation or dysrhythmia or a family history of prolonged QT interval or sudden death.

15. Clinically significant abnormal finding on ECG and/or evidence of any of the following cardiac conduction abnormalities at Screening:

a. Heart rate < 40 bpm and > 100 bpm (based on the ECG reading)

b. QTcF interval > 450 msec for males and females

c. PR interval ≥ 200 msec

d. Intraventricular conduction delay with QRS duration > 120 msec

e. Evidence of second- or third-degree atrioventricular block (AVB)

f. Electrocardiographic evidence of complete left bundle branch block (LBBB), complete right bundle branch block (RBBB), or incomplete LBBB

Revised Wording

A subject will be excluded from the study if he or she meets the following criteria:

1. Are pregnant or lactating.

2. Have a history or presence of significant cardiovascular, respiratory, hepatic, renal, gastrointestinal, endocrine, neurological or psychological/psychiatric disorders which, in the opinion of the Investigator, increases the risk of the study drug or may confound the interpretation of study measures.

3. Clinically significant abnormal findings on physical examination or vital signs as determined by PI.

4. Individuals with pacemakers, aneurysm clips, shrapnel, or other restricted implanted metallic devices will be excluded from study. All subjects complete the standard MRI screening questionnaire prior to MRI.

5. History or presence of psychiatric or neurological disease or condition as determined by the PI.

6. History of seizures.

7. Subject with any history or current evidence of suicidal behavior.

8. Unwilling to complete any planned study assessments.

9. Have a history of blood donation in excess of 500 mL of blood within 30 days prior to Screening.

10. Have received treatment with an investigational drug or device within 30 days prior to Screening.

11. Have a positive test for Human Immunodeficiency Virus (HIV) antibodies 1 and 2, Hepatitis B Surface Antigen (HBsAg) or Hepatitis C Virus (HCV) antibody.

12. Any subject who is known to be allergic to the study drug or any components of the study drug.

13. The subject has a fasting blood glucose ≥ 126 mg/dL or hemoglobin A1c (HbA1c) ≥ 6.5% at Screening.

14. The subject has a history of QT prolongation or dysrhythmia or a family history of prolonged QT interval or sudden death.

15. Clinically significant abnormal finding on ECG and/or evidence of any of the following cardiac conduction abnormalities at Screening:

a. Heart rate < 40 bpm and > 100 bpm (based on the ECG reading)

b. QTcF interval > 450 msec for males and females

c. PR interval ≥ 200 msec

d. Intraventricular conduction delay with QRS duration > 120 msec

e. Evidence of second- or third-degree atrioventricular block (AVB)

f. Electrocardiographic evidence of complete left bundle branch block (LBBB), complete right bundle branch block (RBBB), or incomplete LBBB

16. Any subject who has a positive Urine Drug Screen test on the Day 0 or Day 1 Visit, unless in the Investigator's (PI or Sub-I) documented opinion, the positive test does not signal a clinical condition that would impact the safety of the subject or interpretation of the trial results. The Investigator (PI or Sub-

I) must provide their documented opinion to the Sponsor's Medical Monitor, and then the Sponsor (CMO) within 24 hours of their decision.

17. Any subject who has an Alcohol Breathalyzer test result deemed positive by the Investigator (Principal Investigator or Sub-Investigator) on the Day 0 or Day 1 Visit, unless in the Investigator's (PI or Sub-I) documented opinion, the positive test does not signal a clinical condition that would impact the safety of the subject or interpretation of the trial results. The Investigator (PI or Sub-I) must provide their documented opinion to the Sponsor's Medical Monitor, and then the Sponsor (CMO) within 24 hours of their decision.

Section 1 – Endpoint

<u>Original Wording</u>

LB-102 binding potential and dopamine receptor occupancy measured as amount of 11C raclopride displaced by LB-102 using PET at Screening (baseline), and at 2.5, 7.5, and 23.5 hours post oral dose of LB-102 for Cohorts 1-3. For Cohort 4, one PET scan will be done at Screening (baseline) and three (3) PET scans will be done on Days 5 and 6 (two on Day 5 post LB-102 dose [at times determined following Cohorts 1-3] and one on Day 6 [23.5 h after last LB-102 dose]) in the caudate, putamen, thalamus, and temporal cortex. The cerebellum (devoid of Dopamine D2/D3 receptors) will be used as the reference region. Timing of scans for Cohorts 2-4 may be altered based on observations in Cohort 1.

<u>Revised Wording</u>

*LB-102 binding potential and dopamine receptor occupancy measured as amount of 11C raclopride displaced by LB-102 using PET at **Day 0** (baseline), and at 2.5, 7.5, and 23.5 hours post oral dose of LB-102 for Cohorts 1-3. For Cohort 4, one PET scan will be done at **Day 0** (baseline) and three (3) PET scans will be done on Days 5 and 6 (two on Day 5 post LB-102 dose [at times determined following Cohorts 1-3] and one on Day 6 [23.5 h after last LB-102 dose]) in the caudate, putamen, thalamus, and temporal cortex. The cerebellum (devoid of Dopamine D2/D3 receptors) will be used as the reference region. Timing of scans for Cohorts 2-4 may be altered based on observations in Cohort 1.*

Section 1 – Safety

<u>Original Wording</u>

The following schedule represents the ideal study schedule. It should be used as guidance for study conduct. In the event there are delays at any visit days that may affect the dates of any subsequent visit, the planned days may vary. The following will be monitored to assess safety:

1. AEs:

a. Cohorts 1-3: Days 0-3

b. *Cohort 4: Days 0-7*

2. *Hematology, chemistry, urinalysis at:*

   a. *Cohorts 1-3: Screening, Day 0, and Day 2**

   b. *Cohort 4: Screening, Day 0, and Day 6**

      i. *** - Only blood will be collected for laboratory tests.***

3. *Prolactin at:*

   a. *Cohorts 1-3: Screening and Day 2*

   b. *Cohort 4: Screening and Day 6*

4. *ECG*

   a. *Cohorts 1-3: Screening, Day 0 (prior to PET scan, ±15 min), and Day 2 (24 h post-dose, ±15 min)*

   b. *Cohort 4: Screening, Day 0 (prior to PET scan, ±15 min), and Day 6 (24 h post dose, ±15 min)*

5. *Physical examination*

   a. *Cohorts 1-3: Screening and Day 0**

   b. *Cohort 4: Screening and Days 0**

      i. *** - If physical examination was not performed at Screening then physical examination completed at Day 0***

6. *Vital signs (heart rate, respiratory rate, temperature, and blood pressure)*

   a. *Cohorts 1-3: Screening, Day 0 (at the time of the PET scan, ±15 min), Days 1-2 (Day 1 at pre-dose, and at the time of each PET scan [±15 min, Visits 3 and 4])*

   b. *Cohort 4: Screening, Day 0 (at the time of the PET scan, ±15 min), Days 1-6 (Day 1 at pre-dose, and at the time of each PET scan [±15 min, Visits 3 and 4])*

7. *C-SSRS*

   a. *Cohorts 1-3: Screening and Day 2*

   b. *Cohort 4: Screening and Day 6*

Revised Wording

The following schedule represents the ideal study schedule. It should be used as guidance for study conduct. In the event there are delays at any visit days that may affect the dates of any subsequent visit, the planned days may vary. The following will be monitored to assess safety:

1. *AEs:*
    a. *Cohorts 1-3: Days 0-3*
    b. *Cohort 4: Days 0-7*
2. *Hematology, chemistry, urinalysis at:*
    a. *Cohorts 1-3: Screening, Day 0, and Day 2**
    b. *Cohort 4: Screening, Day 0, and Day 6**
        i. ** - Only blood will be collected for laboratory tests.*
3. *Prolactin at:*
    a. *Cohorts 1-3: Screening and Day 2*
    b. *Cohort 4: Screening and Day 6*
4. *ECG*
    a. *Cohorts 1-3: Screening, Day 0 (prior to PET scan, ±**30** min), and Day 2 (24 h post-dose, ±**30** min)*
    b. *Cohort 4: Screening, Day 0 (prior to PET scan, ±**30** min), and Day 6 (24 h post dose, ±**30** min)*
5. *Physical examination*
    a. *Cohorts 1-3: Screening and Day 0**
    b. *Cohort 4: Screening and Days 0**
        i. ** - If physical examination was not performed at Screening then physical examination completed at Day 0*
6. *Vital signs (heart rate, respiratory rate, temperature, and blood pressure)*
    a. *Cohorts 1-3: Screening, Day 0 (at the time of the PET scan, ±**30** min), Days 1-2 (Day 1 at pre-dose, and at the time of each PET scan [±**30** min, Visits 3 and 4])*
    b. *Cohort 4: Screening, Day 0 (at the time of the PET scan, ±**30** min), Days 1-6 (Day 1 at pre-dose, and at the time of each PET scan [±**30** min, Visits 3 and 4])*

7. *C-SSRS*

   a. *Cohorts 1-3: Screening and Day 2*

   b. *Cohort 4: Screening and Day 6*

Original Wording

Table 1: Schedule of Events, Single Dose Cohorts (Cohorts 1-3)

	Screening	*Pre-Dose Scan*	*Check-In*	*Discharge*	*Follow-Up*	*Pregnancy Follow-Up*
Visit	*1*	*2*	*3*	*4*	*5*	*6*
Days	*Days -14 to -1*	*Day 0*	*Day 1*	*Day 2*	*Day 3*	*Day 31*
Location	*Outpatient*	*Outpatient*	*Inpatient*	*Inpatient/ Outpatient*	*Outpatient*	*Outpatient*
Informed Consent	*X*					
Inclusion/Exclusion Criteria	*X*	*X*				
Medical History	*X*	*X*				
Demographics	*X*					
Height, Weight, BMI	*X*					
Physical Examination[1]	*X*	*X*[1]				
Vital Signs[2]	*X*	*X*	*X*	*X*		
Structural MRI[3]	*X*					
*Laboratory Tests**	*X*	*X*		*X**		
Serum HbA1c	*X*					
Serum Prolactin	*X*			*X*		
HIV, HBsAg, and HCV Labs	*X*					
C-SSRS	*X*			*X*		
12-Lead ECG[4]	*X*	*X*		*X*		
Pregnancy Test[5]	*X*	*X*	*X*	*X*		
Plasma PK[6]			*X*	*X*		
Dose Subjects[7]			*X*			
Concomitant Medication[8]	*X*	*X*	*X*	*X*	*X*	
Adverse Event Assessment[8]		*X*	*X*	*X*	*X*	
PET Scan[9]		*X*	*X*	*X*		
Follow-Up by Telephone[10]				*X*	*X*	*X*

Notes to the Schedule of Events:
BMI = Body Mass Index; ECG = Electrocardiogram; FSH = Follicle-Stimulating Hormone; HbA1c = Hemoglobin A1c; HBsAg = Hepatitis B Surface Antigen; HCV = Hepatitis C Virus; HIV = Human Immunodeficiency Virus; MRI = Magnetic Resonance Imaging; PET = Positron Emission Tomography; PK = Pharmacokinetic

1 If physical examination was not performed at screening then physical examination completed at Day 0.
2 Vital Signs will be measured at Screening, Day 0 (at the time of the PET scan, ±15 min), Day 1 at pre-dose, and at the time of each PET scan (±15 min, Visits 3 and 4).
3 MRI can be done any time before Day 0. An MRI obtained in the prior 6 months for research purposes can substitute for this screening scan.
4 ECG will be measured at Screening, Day 0 (prior to PET scan, ±15 min), and Day 2 (24 h post-dose, ±15 min).
5 Serum pregnancy test at Screening and Urine pregnancy test on Days 0-2 for all females of childbearing potential.
6 Plasma PK samples will be collected at Day 1 at pre-dose, and at the following times post dose (±15 min): 0.5, 1, 2, 4, 8, and 24 h (Day 2).
7 Subjects are required to fast for approximately 12 hours prior to Day 1 dosing.
8 Concomitant Medication and Adverse Event Assessment will be recorded once per day on the days indicated.

[9] For Cohort 1-3 PET scans will be done on Day 0 and 2.5, 7.5, and 23.5 (±30 min) hours post oral dose of LB-102.

[10] Day 2 follow-up call will be done in the evening when the subject returns to their home. Day 3 follow-up call will be done in the morning. The Pregnancy Follow-Up telephone call will only determine whether female subjects of childbearing or the female partner of a male subject (that is not surgically sterile) is pregnant.

* On Day 2, only blood will be collected for laboratory tests.

Revised Wording

Table 1: Schedule of Events, Single Dose Cohorts (Cohorts 1-3)

	Screening	*Pre-Dose Scan*	*Check-In*	*Discharge*	*Follow-Up*	*Pregnancy Follow-Up*
Visit	*1*	*2*	*3*	*4*	*5*	*6*
Days	*Days -14 to -1*	*Day 0*	*Day 1*	*Day 2*	*Day 3*	*Day 31*
Location	*Outpatient*	*Outpatient*	*Inpatient*	*Inpatient/ Outpatient*	*Outpatient*	*Outpatient*
Informed Consent	*X*					
Inclusion/Exclusion Criteria	*X*	*X*				
Medical History	*X*	*X*				
Demographics	*X*					
Height, Weight, BMI	*X*					
Physical Examination[1]	*X*	*X*[1]				
Vital Signs[2]	*X*	*X*	*X*	*X*		
Structural MRI[3]	*X*					
*Laboratory Tests**	*X*	*X**		*X**		
Urine Drug Test[@]	***X***[@]	***X***[@]	***X***[@]			
Alcohol Breathalyzer		***X***	***X***			
Serum HbA1c	*X*					
Serum Prolactin	*X*			*X*		
HIV, HBsAg, and HCV Labs	*X*					
C-SSRS	*X*			*X*		
12-Lead ECG[4]	*X*	*X*		*X*		
Pregnancy Test[5]	*X*	*X*	*X*	*X*		
Plasma PK[6]			*X*	*X*		
Dose Subjects[7]			*X*			
Concomitant Medication[8]	*X*	*X*	*X*	*X*	*X*	
Adverse Event Assessment[8]		*X*	*X*	*X*	*X*	
PET Scan[9]		*X*	*X*	*X*		
Follow-Up by Telephone[10]				*X*	*X*	*X*

Notes to the Schedule of Events:
BMI = Body Mass Index; ECG = Electrocardiogram; FSH = Follicle-Stimulating Hormone; HbA1c = Hemoglobin A1c; HBsAg = Hepatitis B Surface Antigen; HCV = Hepatitis C Virus; HIV = Human Immunodeficiency Virus; MRI = Magnetic Resonance Imaging; PET = Positron Emission Tomography; PK = Pharmacokinetic

1 *If physical examination was not performed at screening then physical examination completed at Day 0.*
2 *Vital Signs will be measured at Screening, Day 0 (at the time of the PET scan, ±**30** min), Day 1 at pre-dose, and at the time of each PET scan (±**30** min, Visits 3 and 4).*
3 *MRI can be done any time before Day 0. An MRI obtained in the prior 6 months for research purposes can substitute for this screening scan.*
4 *ECG will be measured at Screening, Day 0 (prior to PET scan, ±**30** min), and Day 2 (24 h post-dose, ±**30** min).*
5 *Serum pregnancy test at Screening and Urine pregnancy test on Days 0-2 for all females of childbearing potential.*
6 *Plasma PK samples will be collected at Day 1 at pre-dose, and at the following times post dose (±15 min): 0.5, 1, 2, 4, 8, and 24 h (Day 2).*
7 *Subjects are required to fast for approximately 12 hours prior to Day 1 dosing.*

[8] *Concomitant Medication and Adverse Event Assessment will be recorded once per day on the days indicated.*

[9] *For Cohort 1-3 PET scans will be done on Day 0 and 2.5, 7.5, and 23.5 (±30 min) hours post oral dose of LB-102.*

[10] *Day 2 follow-up call will be done in the evening when the subject returns to their home. Day 3 follow-up call will be done in the morning. The Pregnancy Follow-Up telephone call will only determine whether female subjects of childbearing or the female partner of a male subject (that is not surgically sterile) is pregnant.*

* *On Day 2, only blood will be collected for laboratory tests.*

@ Urine Drug Screens will occur at Screening and Days 0-1. On Days 0 and 1, the urine drug screen will be analyzed by the Easy@Home 10 Panel Instant Drug Test Kit.

Original Wording

Table 2: Schedule of Events, Multiple Dose Cohort (Cohort 4)

	Screening	*Pre-Dose Scan*	*Treatment Evaluation*	*Discharge*	*Follow-Up*	*Pregnancy Follow-Up*
Visit	*1*	*2*	*3*	*4*	*5*	*6*
Days	*Days -14 to -1*	*Day 0*	*Days 1-5*	*Day 6*	*Day 7*	*Day 35*
Location	*Outpatient*	*Outpatient*	*Inpatient*	*Inpatient/ Outpatient*	*Outpatient*	*Outpatient*
Informed Consent	*X*					
Inclusion/Exclusion Criteria	*X*	*X*				
Medical History	*X*	*X*				
Demographics	*X*					
Height, Weight, BMI[1]	*X*					
Physical Examination	*X*	*X*[1]				
Vital Signs[2]	*X*	*X*	*X*	*X*		
*Laboratory Tests**	*X*	*X*		*X**		
Structural MRI[3]	*X*					
Serum HbA1c	*X*					
Serum Prolactin	*X*			*X*		
HIV, HBsAg, and HCV Labs	*X*					
C-SSRS	*X*			*X*		
12-Lead ECG[4]	*X*	*X*		*X*		
Pregnancy Test[5]	*X*	*X*	*X (Day 5)*	*X*		
Plasma PK[6]			*X*	*X*		
Dose Subjects[7]			*X*			
Concomitant Medication[8]	*X*	*X*	*X*	*X*	*X*	
Adverse Event Assessment		*X*	*X*	*X*	*X*	
PET scan[9]		*X*	*X*	*X*		
Follow up by telephone[10]				*X*	*X*	*X*

Notes to the Schedule of Events:

BMI = Body Mass Index; ECG = Electrocardiogram; FSH = Follicle-Stimulating Hormone; HbA1c = Hemoglobin A1c; HBsAg = Hepatitis B Surface Antigen; HCV = Hepatitis C Virus; HIV = Human Immunodeficiency Virus; MRI = Magnetic Resonance Imaging; PET = Positron Emission Tomography; PK = Pharmacokinetic

1 If physical examination was not performed at screening then physical examination completed at Day 0.

2 Vital Signs will be measured at Screening, Day 0 (at the time of the PET scan, ±15 min), Day 1 at pre-dose, and at the time of each PET scan (±15 min, Visits 3 and 4).

3 MRI can be done any time before Day 0. An MRI obtained in the prior 6 months for research purposes can substitute for this screening scan.

4 ECG will be measured at Screening, Day 0 (prior to PET scan, ±15 min) and after scan 4 (24 h post-dose, ±15 min).

5 Serum pregnancy test at Screening and Urine pregnancy test on Days 0, 5, and 6 for all females of childbearing potential.

[6] Plasma PK samples will be collected on Day 1 at pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, 8, and 24 h (Day 2). Plasma PK samples will also be collected on Day 5 immediately pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, 8, and 24 h (Day 6)

[7] Subjects are required to fast for approximately 12 hours prior to the first Day 1 dose. On Days 1-4, subjects will receive 2 doses per day (8 AM and 8 PM ±1 hour) separated by approximately 12 hours. On Day 5, subjects will receive 1 dose (8 AM ±1 hour).

[8] Concomitant Medication and Adverse Event Assessment will be recorded once per day on the days indicated.

[9] One PET scan will be done on Day 0. Three PET scans will be done on Days 5 and 6, two on Day 5 post LB-102 dose (at times TBD based on first 3 cohorts) and one on Day 6 23.5 h after last LB-102 dose.

[10] Day 6 follow-up call will be done in the evening when the subject returns to their home. Day 7 follow-up call will be done in the morning. The Pregnancy Follow-Up telephone call will only determine whether female subjects of childbearing or the female partner of a male subject (that is not surgically sterile) is pregnant.

* On Day 6, only blood will be collected for laboratory tests.

Revised Wording

Table 2: Schedule of Events, Multiple Dose Cohort (Cohort 4)

	Screening	*Pre-Dose Scan*	*Treatment Evaluation*	*Discharge*	*Follow-Up*	*Pregnancy Follow-Up*
Visit	*1*	*2*	*3*	*4*	*5*	*6*
Days	*Days -14 to -1*	*Day 0*	*Days 1-5*	*Day 6*	*Day 7*	*Day 35*
Location	*Outpatient*	*Outpatient*	*Inpatient*	*Inpatient/ Outpatient*	*Outpatient*	*Outpatient*
Informed Consent	*X*					
Inclusion/Exclusion Criteria	*X*	*X*				
Medical History	*X*	*X*				
Demographics	*X*					
Height, Weight, BMI[1]	*X*					
Physical Examination	*X*	*X*[1]				
Vital Signs[2]	*X*	*X*	*X*	*X*		
*Laboratory Tests**	*X*	*X**		*X**		
Urine Drug Screen@	***X***[@]	***X***[@]	***X***[@] ***(Day 1)***			
Alcohol Breathalyzer		***X***	***X (Day 1)***			
Structural MRI[3]	*X*					
Serum HbA1c	*X*					
Serum Prolactin	*X*			*X*		
HIV, HBsAg, and HCV Labs	*X*					
C-SSRS	*X*			*X*		
12-Lead ECG[4]	*X*	*X*		*X*		
Pregnancy Test[5]	*X*	*X*	*X (Day 5)*	*X*		
Plasma PK[6]			*X*	*X*		
Dose Subjects[7]			*X*			
Concomitant Medication[8]	*X*	*X*	*X*	*X*	*X*	
Adverse Event Assessment		*X*	*X*	*X*	*X*	
PET scan[9]		*X*	*X*	*X*		
Follow up by telephone[10]				*X*	*X*	*X*

Notes to the Schedule of Events:

BMI = Body Mass Index; ECG = Electrocardiogram; FSH = Follicle-Stimulating Hormone; HbA1c = Hemoglobin A1c; HBsAg = Hepatitis B Surface Antigen; HCV = Hepatitis C Virus; HIV = Human Immunodeficiency Virus; MRI = Magnetic Resonance Imaging; PET = Positron Emission Tomography; PK = Pharmacokinetic

1 *If physical examination was not performed at screening then physical examination completed at Day 0.*

2 *Vital Signs will be measured at Screening, Day 0 (at the time of the PET scan, ±**30** min), Day 1 at pre-dose, and at the time of each PET scan (±**30** min, Visits 3 and 4).*

3 *MRI can be done any time before Day 0. An MRI obtained in the prior 6 months for research purposes can substitute for this screening scan.*

[4] *ECG will be measured at Screening, Day 0 (prior to PET scan, ±**30** min) and **Day 6** (24 h post-dose, ±**30** min).*

[5] *Serum pregnancy test at Screening and Urine pregnancy test on Days 0, 5, and 6 for all females of childbearing potential.*

[6] *Plasma PK samples will be collected on Day 1 at pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, 8, and 24 h (Day 2). Plasma PK samples will also be collected on Day 5 immediately pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, 8, and 24 h (Day 6)*

[7] *Subjects are required to fast for approximately 12 hours prior to the first Day 1 dose. On Days 1-4, subjects will receive 2 doses per day (**9** AM and **9** PM ±1 hour) separated by approximately 12 hours. On Day 5, subjects will receive 1 dose (**9** AM ±1 hour).*

[8] *Concomitant Medication and Adverse Event Assessment will be recorded once per day on the days indicated.*

[9] *One PET scan will be done on Day 0. Three PET scans will be done on Days 5 and 6, two on Day 5 post LB-102 dose (at times TBD based on first 3 cohorts) and one on Day 6 (23.5 h after last LB-102 dose).*

[10] *Day 6 follow-up call will be done in the evening when the subject returns to their home. Day 7 follow-up call will be done in the morning. The Pregnancy Follow-Up telephone call will only determine whether female subjects of childbearing or the female partner of a male subject (that is not surgically sterile) is pregnant.*

* *On Day 6, only blood will be collected for laboratory tests.*

@ **Urine Drug Screens will occur at Screening and on Days 0 and 1. On Days 0 and 1, the urine drug screen will be analyzed by the Easy@Home 10 Panel Instant Drug Test Kit.**

Section 5.2.2 – Exclusion Criteria

<u>Original Wording</u>

A subject will be excluded from the study if he or she meets the following criteria:

1. Are pregnant or lactating.

2. Have a history or presence of significant cardiovascular, respiratory, hepatic, renal, gastrointestinal, endocrine, neurological or psychological/psychiatric disorders which, in the opinion of the Investigator, increases the risk of the study drug or may confound the interpretation of study measures.

3. Clinically significant abnormal findings on physical examination or vital signs as determined by PI.

4. Individuals with pacemakers, aneurysm clips, shrapnel, or other restricted implanted metallic devices will be excluded from study. All subjects complete the standard MRI screening questionnaire prior to MRI.

5. History or presence of psychiatric or neurological disease or condition as determined by the PI.

6. History of seizures.

7. Subject with any history or current evidence of suicidal behavior.

8. Unwilling to complete any planned study assessments.

9. Have a history of blood donation in excess of 500 mL of blood within 30 days prior to Screening.

10. Have received treatment with an investigational drug or device within 30 days prior to Screening.

11. Have a positive test for Human Immunodeficiency Virus (HIV) antibodies 1 and 2, Hepatitis B Surface Antigen (HBsAg) or Hepatitis C Virus (HCV) antibody.

12. Any subject who is known to be allergic to the study drug or any components of the study drug.

13. The subject has a fasting blood glucose ≥ 126 mg/dL or hemoglobin A1c (HbA1c) ≥ 6.5% at Screening.

14. The subject has a history of QT prolongation or dysrhythmia or a family history of prolonged QT interval or sudden death.

15. Clinically significant abnormal finding on ECG and/or evidence of any of the following cardiac conduction abnormalities at Screening:

a. Heart rate < 40 bpm and > 100 bpm (based on the ECG reading)

b. QTcF interval > 450 msec for males and females

c. PR interval ≥ 200 msec

d. Intraventricular conduction delay with QRS duration > 120 msec

e. Evidence of second- or third-degree atrioventricular block (AVB)

f. Electrocardiographic evidence of complete left bundle branch block (LBBB), complete right bundle branch block (RBBB), or incomplete LBBB

Revised Wording

A subject will be excluded from the study if he or she meets the following criteria:

1. Are pregnant or lactating.

2. Have a history or presence of significant cardiovascular, respiratory, hepatic, renal, gastrointestinal, endocrine, neurological or psychological/psychiatric disorders which, in the opinion of the Investigator, increases the risk of the study drug or may confound the interpretation of study measures.

3. Clinically significant abnormal findings on physical examination or vital signs as determined by PI.

4. Individuals with pacemakers, aneurysm clips, shrapnel, or other restricted implanted metallic devices will be excluded from study. All subjects complete the standard MRI screening questionnaire prior to MRI.

5. History or presence of psychiatric or neurological disease or condition as determined by the PI.

6. History of seizures.

7. Subject with any history or current evidence of suicidal behavior.

8. Unwilling to complete any planned study assessments.

9. Have a history of blood donation in excess of 500 mL of blood within 30 days prior to Screening.

10. Have received treatment with an investigational drug or device within 30 days prior to Screening.

11. Have a positive test for Human Immunodeficiency Virus (HIV) antibodies 1 and 2, Hepatitis B Surface Antigen (HBsAg) or Hepatitis C Virus (HCV) antibody.

12. Any subject who is known to be allergic to the study drug or any components of the study drug.

13. The subject has a fasting blood glucose ≥ 126 mg/dL or hemoglobin A1c (HbA1c) ≥ 6.5% at Screening.

14. The subject has a history of QT prolongation or dysrhythmia or a family history of prolonged QT interval or sudden death.

15. Clinically significant abnormal finding on ECG and/or evidence of any of the following cardiac conduction abnormalities at Screening:

a. Heart rate < 40 bpm and > 100 bpm (based on the ECG reading)

b. QTcF interval > 450 msec for males and females

c. PR interval ≥ 200 msec

d. Intraventricular conduction delay with QRS duration > 120 msec

e. Evidence of second- or third-degree atrioventricular block (AVB)

f. Electrocardiographic evidence of complete left bundle branch block (LBBB), complete right bundle branch block (RBBB), or incomplete LBBB

16. Any subject who has a positive Urine Drug Screen test on the Day 0 or Day 1 Visit, unless in the Investigator's (PI or Sub-I) documented opinion, the positive test does not signal a clinical condition that would impact the safety of the subject or interpretation of the trial results. The Investigator (PI or Sub-I) must provide their documented opinion to the Sponsor's Medical Monitor, and then the Sponsor (CMO) within 24 hours of their decision.

17. Any subject who has an Alcohol Breathalyzer test result deemed positive by the Investigator (Principal Investigator or Sub-Investigator) on the Day 0 or Day 1 Visit, unless in the Investigator's (PI or Sub-I) documented opinion, the positive test does not signal a clinical condition that would impact the safety of the subject or interpretation of the trial results. The Investigator (PI or Sub-I) must provide their documented opinion to the Sponsor's Medical Monitor, and then the Sponsor (CMO) within 24 hours of their decision.

Section 6.3 – Treatment Administration

<u>Original Wording</u>

Subjects will be dispensed LB-102 capsule(s) based on their assigned treatment at 8 AM (±1 hour). Subjects will take the capsule orally with 240 mL of water. Site personnel will confirm that the capsule has been taken by the study subject.

<u>Revised Wording</u>

*Subjects **from Cohorts 1-3** will be dispensed LB-102 capsule(s) based on their assigned treatment at **9** AM (±1 hour) **on Day 1. For Cohort 4, subjects will receive LB-102 capsules BID at 9 AM and 9 PM (±1 hour) from Days 1-4, and once at 9 AM (±1 hour) on Day 5**. Subjects will take the capsule orally with 240 mL of water. Site personnel will confirm that the capsule has been taken by the study subject.*

Section 7.1.2 – Pre-Dose Scan (Visit 2, Day 0)

<u>Original Wording</u>

The following procedures will be performed:

- *Record medical history.*
- *Review inclusion and exclusion criteria.*
- *Physical examination (If physical examination was not performed at Screening).*
- *Vital signs (at the time of the PET scan, ±15 min).*
- *Collect blood and urine samples for clinical laboratory tests (hematology, clinical chemistry, urinalysis, and urine drug screen).*
- *12-lead ECG (prior to PET scan, ±15 min).*
- *Urine pregnancy test for all females of childbearing potential.*
- *Record concomitant medication use.*
- *Assess and record AEs.*
- *Undergo pre-dose PET/CT scan (scan 1)*

<u>Revised Wording</u>

The following procedures will be performed:

- *Record medical history.*
- ~~***Review inclusion and exclusion criteria.***~~
- *Physical examination (If physical examination was not performed at Screening).*
- *Vital signs (at the time of the PET scan, ±**30** min).*
- *Collect blood and urine samples for clinical laboratory tests (hematology, clinical chemistry, urinalysis, and urine drug screen*****).*
    - ****The Pre-Dose Scan Visit urine drug screen will be analyzed by the Easy@Home 10 Panel Instant Drug Test Kit.***
- *12-lead ECG (prior to PET scan, ±**30** min).*

- *Urine pregnancy test for all females of childbearing potential.*
- ***Alcohol Breathalyzer***
- *Record concomitant medication use.*
- *Assess and record AEs.*
- *Undergo pre-dose PET/CT scan (scan 1)*

Section 7.1.3 – Check-In (Visit 3, Day 1)

<u>Original Wording</u>

The following procedures will be performed on Day 1:

- *Administer dose of study drug.*
- *Vital Signs (at pre-dose and at time of each PET scan, ±15 min).*
- *Undergo post-dose PET/CT scan (scan 2) starting at 2.5 hours post LB-102 dose (±30 min).*
- *Undergo post-dose PET/CT scan (scan 3) starting at 7.5 hours post LB-102 dose (±30 min).*
- *Plasma samples for PK analysis pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, and 8 h.*
- *Urine pregnancy test for all females of childbearing potential.*
- *Record concomitant medication use.*
- *Assess and record AEs if reported.*
- *Subjects will be monitored on an in-patient basis beginning on Day 1 until completion of the final scan on Day 2.*

<u>Revised Wording</u>

The following procedures will be performed on Day 1:

- ***Alcohol Breathalyzer***
- ***Urine Drug Screen***
    - ***The Day 1 urine drug screen will be analyzed by the Easy@Home 10 Panel Instant Drug Test Kit.***

- ***Review inclusion and exclusion criteria.***
- *Administer dose of study drug.*
- *Vital Signs (at pre-dose and at time of each PET scan, ±**30** min).*
- *Undergo post-dose PET/CT scan (scan 2) starting at 2.5 hours post LB-102 dose (±30 min).*
- *Undergo post-dose PET/CT scan (scan 3) starting at 7.5 hours post LB-102 dose (±30 min).*
- *Plasma samples for PK analysis pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, and 8 h.*
- *Urine pregnancy test for all females of childbearing potential.*
- *Record concomitant medication use.*
- *Assess and record AEs if reported.*
- *Subjects will be monitored on an in-patient basis beginning on Day 1 until completion of the final scan on Day 2.*

Section 7.1.4 – Discharge (Visit 4, Day 2)

<u>Original Wording</u>

The following procedures will be performed on Day 2:

- *Vital Signs (at the time of the PET scan ±15 min).*
- *12-lead ECG after Scan 4 (24 h post-dose, ±15 min).*
- *Undergo post-dose PET/CT scan (scan 4) starting at 23.5 hours (±30 min) post LB-102 dose.*
- *Plasma samples for PK analysis at the following time post dose (±15 min): 24 h*
- *Collect blood samples for clinical laboratory tests (hematology, clinical chemistry, and serum prolactin).*
- *Urine pregnancy test for all females of childbearing potential.*
- *Record concomitant medication use.*
- *Assess and record AEs if reported.*
- *C-SSRS*

- *Follow-up telephone call.*

Revised Wording

The following procedures will be performed on Day 2:

- *Vital Signs (at the time of the PET scan ±**30** min).*
- *12-lead ECG ~~**after Scan 4**~~ (24 h post-dose, ±**30** min).*
- *Undergo post-dose PET/CT scan (scan 4) starting at 23.5 hours (±30 min) post LB-102 dose.*
- *Plasma samples for PK analysis at the following time post dose (±15 min): 24 h*
- *Collect blood samples for clinical laboratory tests (hematology, clinical chemistry, and serum prolactin).*
- *Urine pregnancy test for all females of childbearing potential.*
- *Record concomitant medication use.*
- *Assess and record AEs if reported.*
- *C-SSRS*
- *Follow-up telephone call.*

Section 7.2.2 – Pre-Dose Scan (Visit 2, Day 0)

Original Wording

The following procedures will be performed:

- *Record medical history.*
- *Review inclusion and exclusion criteria.*
- *Physical examination (If physical examination was not performed at Screening).*
- *Vital signs (at the time of the PET scan, ±15 min).*
- *Collect blood and urine samples for clinical laboratory tests (hematology, clinical chemistry, urinalysis, and urine drug screen).*
- *12-lead ECG (prior to PET scan, ±15 min).*

- *Urine pregnancy test for all females of childbearing potential.*
- *Record concomitant medication use.*
- *Assess and record AEs.*
- *Undergo pre-dose PET/CT scan (scan 1)*

Revised Wording

The following procedures will be performed:

- *Record medical history.*
- ~~***Review inclusion and exclusion criteria.***~~
- *Physical examination (If physical examination was not performed at Screening).*
- *Vital signs (at the time of the PET scan, ±**30** min).*
- *Collect blood and urine samples for clinical laboratory tests (hematology, clinical chemistry, urinalysis, and urine drug screen*****).*
    - ****The Pre-Dose Scan Visit urine drug screen will be analyzed by the Easy@Home 10 Panel Instant Drug Test Kit.***
- *12-lead ECG (prior to PET scan, ±**30** min).*
- *Urine pregnancy test for all females of childbearing potential.*
- ***Alcohol Breathalyzer***
- *Record concomitant medication use.*
- *Assess and record AEs.*
- *Undergo pre-dose PET/CT scan (scan 1)*

Section 7.2.3 – Treatment Administration (Visit 3, Day 1)

Original Wording

The following procedures will be performed on Days 1-5:

- *Dosing at 8 AM and 8 PM (±1 hour) intervals on Days 1-5 (AM only on Day 5).*

- *Vital signs (at pre-dose and at time of each PET scan, ±15 min).*
- *Urine pregnancy test for all females of childbearing potential (Day 5 only).*
- *Record concomitant medication use (prior to first dose on All Days).*
- *Assess and record AEs (prior to first dose on All Days).*
- *Undergo post-dose PET/CT scan (scan 2; TBD, dependent on data from Cohorts 1-3)*
- *Undergo post-dose PET/CT scan (scan 3; TBD, dependent on data from Cohorts 1-3)*
- *Subjects will be monitored on an in-patient basis beginning on Day 1 until completion of the final scan on Day 6*
- *On Day 1 plasma samples for PK analysis at pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, 8, and 24 h (Day 2).*
- *On Day 5 plasma samples for PK analysis at pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, and 8 h.*

Revised Wording

The following procedures will be performed on Days 1-5:

- ***Alcohol Breathalyzer (Day 1).***
- ***Urine Drug Screen (Day 1).***
  - ***The Day 1 urine drug screen will be analyzed by the Easy@Home 10 Panel Instant Drug Test Kit.***
- ***Review inclusion and exclusion criteria (Day 1).***
- *Dosing at **9** AM and **9** PM (±1 hour) intervals on Days 1-5 (AM only on Day 5).*
- *Vital signs (at pre-dose and at time of each PET scan, ±**30** min).*
- *Urine pregnancy test for all females of childbearing potential (Day 5 only).*
- *Record concomitant medication use (prior to first dose on All Days).*
- *Assess and record AEs (prior to first dose on All Days).*
- *Undergo post-dose PET/CT scan (scan 2; TBD, dependent on data from Cohorts 1-3)*
- *Undergo post-dose PET/CT scan (scan 3; TBD, dependent on data from Cohorts 1-3)*

- *Subjects will be monitored on an in-patient basis beginning on Day 1 until completion of the final scan on Day 6*

- *On Day 1 plasma samples for PK analysis at pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, 8, and 24 h (Day 2).*

- *On Day 5 plasma samples for PK analysis at pre-dose and at the following times post dose (±15 min): 0.5, 1, 2, 4, and 8 h.*

Section 7.2.4 – Discharge (Visit 4, Day 6)

Original Wording

The following procedures will be performed on Day 6:

- *Vital signs (at the time of the PET scan, ±15 min).*

- *Undergo post-dose PET/CT scan (scan 4; 23.5 h (±30 min) post LB-102 dose).*

- *12-lead ECG after Scan 4 (24 h post-dose, ±15 min).*

- *On Day 6 plasma samples for PK analysis at the following times post dose (±15 min): 24 h.*

- *Collect blood samples for clinical laboratory tests (hematology, clinical chemistry, and serum prolactin).*

- *Urine pregnancy test for all females of childbearing potential.*

- *C-SSRS*

- *Record concomitant medication use.*

- *Assess and record AEs.*

- *Follow-up telephone call.*

Revised Wording

The following procedures will be performed on Day 6:

- *Vital signs (at the time of the PET scan, ±**30** min).*

- *Undergo post-dose PET/CT scan (scan 4; 23.5 h (±30 min) post LB-102 dose).*

- *12-lead ECG ~~**after Scan 4**~~ (24 h post-dose, ±**30** min).*

- *On Day 6 plasma samples for PK analysis at the following times post dose (±15 min): 24 h.*

- *Collect blood samples for clinical laboratory tests (hematology, clinical chemistry, and serum prolactin).*

- *Urine pregnancy test for all females of childbearing potential.*

- *C-SSRS*

- *Record concomitant medication use.*

- *Assess and record AEs.*

- *Follow-up telephone call.*

Section 8.2 – Dopamine Occupancy

<u>Original Wording</u>

LB-102 binding potential and dopamine receptor occupancy will be measured as the amount of 11C Raclopride displaced by LB-102 using PET at Screening (baseline), and at 2.5, 7.5, and 23.5 hours post oral dose of LB-102 for Cohorts 1-3. For Cohort 4, one PET scan will be done at Screening (baseline) and three (3) PET scans will be done on Days 5 and 6 (two on Day 5 post LB-102 dose [at times determined following Cohorts 1-3] and one on Day 6 [23.5 h after last LB-102 dose]) in the caudate, putamen, thalamus, and temporal cortex. The cerebellum (devoid of Dopamine D2/D3 receptors) will be used as a reference region. Timing of scans for Cohorts 2-4 may be altered based on observations in Cohort 1.

Dopamine D2 receptor occupancy (D2occ) after the 2nd 3rd and 4th scans will be expressed as percent change in the ratio of the BPND at baseline (scan 1 with no drug) vs the BPND after scan 2 , scan 3, and scan 4.

<u>Revised Wording</u>

*LB-102 binding potential and dopamine receptor occupancy will be measured as the amount of 11C Raclopride displaced by LB-102 using PET at **Day 0** (baseline), and at 2.5, 7.5, and 23.5 hours post oral dose of LB-102 for Cohorts 1-3. For Cohort 4, one PET scan will be done at **Day 0** (baseline) and three (3) PET scans will be done on Days 5 and 6 (two on Day 5 post LB-102 dose [at times determined following Cohorts 1-3] and one on Day 6 [23.5 h after last LB-102 dose]) in the caudate, putamen, thalamus, and temporal cortex. The cerebellum (devoid of Dopamine D2/D3 receptors) will be used as a reference region. Timing of scans for Cohorts 2-4 may be altered based on observations in Cohort 1.*

Dopamine D2 receptor occupancy (D2occ) after the 2nd 3rd and 4th scans will be expressed as percent change in the ratio of the BPND at baseline (scan 1 with no drug) vs the BPND after scan 2 , scan 3, and scan 4.

Section 8.6.2.3 Reporting Adverse Events

Original Wording

Role in Study	***Name***	***Address and Telephone Number***
Medical Monitor	*Anna Eramo, MD*	*LB Pharmaceuticals, Inc.* *575 Madison Ave., 10th Floor* *New York, NY 10022* *Email: anna@lbpharma.us* *Phone: 312-661-2021*
Medical Monitor	*Bruce Reidenberg, MD, FAAP, FCP*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: breidenberg@gmail.com* *Phone: 914-707-4195*
Safety Monitor	*Luxi Wang, PharmD*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: luwang@targethealth.com* *Phone: 917-660-2597*

Revised Wording

Role in Study	***Name***	***Address and Telephone Number***
Medical Monitor ***(Primary Contact)***	*Bruce Reidenberg, MD, FAAP, FCP*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: breidenberg@gmail.com* *Phone: 914-707-4195*
Medical Monitor ***(Secondary Contact)***	*Anna Eramo, MD*	*LB Pharmaceuticals, Inc.* *575 Madison Ave., 10th Floor* *New York, NY 10022* *Email: anna@lbpharma.us* *Phone: 312-661-2021*
Safety Monitor	*Luxi Wang, PharmD*	*Target Health LLC.* *261 Madison Ave, 24th Floor* *New York, NY 10016* *Email: luwang@targethealth.com* *Phone: 917-660-2597*

Section 8.6.4 – Laboratory Safety Assessment

<u>Original Wording</u>

Samples for the following laboratory tests will be collected at the time points specified in the Schedule of Events (Table 1 and Table 2).

Hematology:	*Consists of complete blood count (hemoglobin, hematocrit, white blood cell count with differential, red blood cell count, and platelet count)*
Serum Chemistry:	*Includes blood urea nitrogen, creatinine, total bilirubin, alkaline phosphatase, aspartate aminotransferase (serum glutamic-oxaloacetic transaminase), alanine aminotransferase (serum glutamic pyruvic transaminase), glucose, HbA1c*, albumin, prolactin, and total protein*
Urinalysis:	*Includes pH, specific gravity, protein, glucose, ketones, bilirubin, blood, nitrites, leukocytes, urobilinogen, microscopic urine analysis if dipstick positive*
Serum and Urine Pregnancy Test:*	*Conducted for females of childbearing potential only*
FSH	*Postmenopausal females (at screening only)*
Urine Drug Screen:	*Cocaine, amphetamine, phencyclidine, benzodiazepines, opiates, and marijuana.*

**Serum for pregnancy test and HbA1c assessment are only required at Screening.*

Serum prolactin values ≥ 100 ng/mL will be considered clinically significant and recorded as an AE. Serum prolactin values greater than the normal reference range value but < 100 ng/mL will not be considered clinically significant.

<u>Revised Wording</u>

Samples for the following laboratory tests will be collected at the time points specified in the Schedule of Events (Table 1 and Table 2).

Hematology:	*Consists of complete blood count (hemoglobin, hematocrit, white blood cell count with differential, red blood cell count, and platelet count)*
Serum Chemistry:	*Includes blood urea nitrogen, creatinine, total bilirubin, alkaline phosphatase, aspartate aminotransferase (serum glutamic-oxaloacetic*

	transaminase), alanine aminotransferase (serum glutamic pyruvic transaminase), glucose, HbA1c, albumin, prolactin, and total protein*
Urinalysis:	*Includes pH, specific gravity, protein, glucose, ketones, bilirubin, blood, nitrites, leukocytes, **~~urobilinogen,~~** microscopic urine analysis if dipstick positive*
Serum and Urine Pregnancy Test:*	*Conducted for females of childbearing potential only*
FSH	*Postmenopausal females (at screening only)*
Urine Drug Screen:	*Cocaine, amphetamine, phencyclidine, benzodiazepines, opiates, and marijuana.*

**Serum for pregnancy test and HbA1c assessment are only required at Screening.*

Serum prolactin values ≥ 100 ng/mL will be considered clinically significant and recorded as an AE. Serum prolactin values greater than the normal reference range value but < 100 ng/mL will not be considered clinically significant.

For the Day 0 and Day 1 urine drug screens, the Easy@Home 10 Panel Instant Drug Test Kit (EDOAP-3104; 510K Number: K133968, 2014, Guangzhou Wondfo Biotech Co., Ltd) will be used to analyze the urine drug screen sample. Instructions for use can be found in Section 14.1 (Appendix 1).

New Section Added

Section 14 Appendices

Section 14.1 - Easy@Home Drug Test Brochure

pharmaceuticals

easy@Home®

Multi Drug Screen Test

Easy@Home Multi Drug Screen Test offers any combination from 2 to 15 drugs of abuse tests for 15 different drugs: Amphetamine (AMP), Barbiturates (BAR), Benzodiazepines (BZO), Cocaine (COC), Marijuana (THC), Methadone (MTD), Methamphetamine (MET), Methylenedioxymethamphetamine(MDMA), Morphine (MOP), Opiate (OPI 2000), Phencyclidine (PCP), Tricyclic Antidepressants (TCA), Buprenorphine (BUP), Oxycodone (OXY), Propoxyphene (PPX).

This package insert applies to all Multi Drug Screen Test. Therefore, some information on the performance characteristics of the product may not be relevant to your test. Please refer to the labels on the packaging and the prints on the test strip to identify which drugs are included in your test.

A rapid one step test for the qualitative detection of drug of abuse and their principal metabolites in human urine at specified cut off level.

For in vitro diagnostic use only. For over-the-counter use only.

INTENDED USE

Easy@Home Multi Drug Screen Test is rapid urine screening test. The test is a lateral flow, one-step immunoassay for the qualitative detection of specific drugs and their metabolites in human urine at the following cut off concentrations:

Drug(Identifier)	Calibrator	Cut-off level	Minimum detection time	Maximum detection time
Amphetamine (AMP)	d-Amphetamine	1000ng/mL	2-7 hours	1-2 days
Barbiturates (BAR)	Secobarbital	300 ng/mL	2-4 hours	1-4 days
Benzodiazepine (BZO)	Oxazepam	300 ng/mL	2-7 hours	1-2 days
Buprenorphine(BUP)	Buprenorphine	10 ng/mL	4 hours	1-3 days
Cocaine (COC)	Benzoylecgonine	300 ng/mL	1-4 hours	2-4 days
Marijuana (THC)	11-nor-Δ9-THC-9-COOH	50 ng/mL	2 hours	Up to 5+ days
Methadone (MTD)	Methadone	300 ng/mL	3-8 hours	1-3 days
Methamphetamine (MET)	D(+)-Methamphetamine	1000ng/mL	2-7 hours	2-4 days
Methylenedioxymethamphetamine (MDMA)	3,4-Methylenedioxymethamphetamine HCl (MDMA)	500 ng/mL	2-7 hours	2-4 days
Morphine (MOP)	Morphine	300 ng/mL	2 hours	2-3 days
Opiate (OPI2000)	Morphine	2000ng/mL	2 hours	2-3 days
Oxycodone(OXY)	Oxycodone	100 ng/mL	4 hours	1-3 days
Phencyclidine (PCP)	Phencyclidine	25 ng/mL	4-6 hours	7-14days
Propoxyphene(PPX)	Propoxyphene	300 ng/mL	8-12hours	5-10days
Tricyclic Antidepressants (TCA)	Notriptyline	1000ng/mL	8-12hours	2-7 days

This assay provides only a preliminary test result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary results are positive.

PRINCIPLE

DRUG TESTS

Easy@Home Multi Drug Screen Test is a competitive immunoassay that is used to screen for the presence of drugs of abuse in urine. It is chromatographic absorbent device in which drugs or drug metabolites in a sample competitively combined to a limited number of antibody-dye conjugate binding sites.

When testing, the urine is absorbed upward by capillary action, mixes with the antibody-dye conjugate, and flows across the pre-coated membrane.

When sample drug levels are at or above the target cutoff, the drug in the sample binds to the antibody-dye conjugate preventing the antibody-dye conjugate from binding to the drug-protein pre-coated in the test region (T). This prevents the development of a distinct colored band in the test region indicating a potentially positive result.

When sample drug levels are zero or below the target cutoff (the detection sensitivity of the test), antibody-dye conjugate binds to the drug-protein pre-coated in the test region (T) of the device. This produces a colored test line that, regardless of its intensity, indicates a negative result.

To serve as a procedure control, a colored line will appear on the control region (C), if the test has been performed properly.

WARNINGS AND PRECAUTIONS

- This kit is for external use only. Do not swallow.
- Discard after first use. The test cannot be used more than once.
- Do not use test kit beyond expiration date.
- Do not use the kit if the pouch is punctured or not well sealed.
- Keep out of the reach of children.

STORAGE AND STABILITY

- Store at 4°C-30°C (40°F-86°F) up to the expiration date.
- Keep away from sunlight, moisture and heat.
- DO NOT FREEZE.

pharmaceuticals

MATERIAL

Material provided

- One pouch containing a test panel and a desiccant.
- Package insert

Material Required But Not Provided

- Timer
- Urine cup

SPECIMEN COLLECTION AND PREPARATION

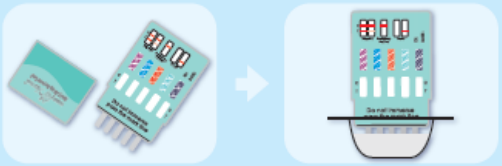
Collect a urine sample in the urine cup. Urine specimens may be refrigerated 2°C-8°C (36°F-47°F) and stored up to forty-eight hours. For longer storage, freeze the samples at -20°C (-4°F) or below. Bring frozen or refrigerated samples to room temperature before testing. Use only clear aliquots for testing.

TEST PROCEDURE

Test must be in room temperature 10°C-30°C (50°F-86°F).

1. Open the sealed pouch by tearing along the notch. Remove the test device from the pouch.
2. Hold the one side of the device with one hand. Use the other hand to pull out the cap and expose the absorbent end.
3. Immerse the absorbent end into the urine sample about 10 seconds. Make sure that the urine level is not above the "MAX" line printed on the front of the device.
4. Lay the device flat on a clean, dry, non-absorbent surface.
5. Read the result at 5 minutes. Do not read after 5 minutes.

Step 1:
Pull the cap off and immerse the strips into urine for 10 seconds

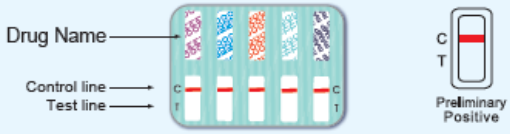


Step 2:
Read the result at 5 minutes. Do not read after 5 minutes.

INTERPRETATION OF RESULTS

Positive (+)

A rose-pink band is visible in each control region. No color band appears in the appropriate test region. It indicates a positive result for the corresponding drug of that specific test zone.



Negative (-)

A rose-pink band is visible in each control region and the appropriate test region. It indicates that the concentration of the corresponding drug of that specific test zone is zero or below the detection limit of the test.

Invalid

If a color band is not visible in each of the control region or a color band is only visible in each of the test region, the test is invalid. Another test should be run to re-evaluate the specimen. Please contact the distributor or the store, where you bought the product, with the lot number.

Note: There is no meaning attributed to line color intensity or width.

pharmaceuticals

QUALITY CONTROL

Users should follow the appropriate federal state, and local guidelines concerning the frequency of assaying external quality control materials. Though there is an internal procedural control line in the test device of control region, the use of external controls is strongly recommended as good laboratory testing practice to confirm the test procedure and to verify proper test performance. Positive and negative controls should give the expected results. When testing the positive and negative controls, the same assay procedure should be adopted.

SPECIFICITY AND CROSS REACTIVITY

To test the specificity of the test, the test device was used to test various drugs, drug metabolites and other components of the same class that are likely to be present in urine. All the components were added to drug-free normal human urine. The following structurally related compounds produced positive results with the test when tested at levels equal to or greater than the concentrations listed below.

Amphetamine (AMP)	Concentration (ng/ml)	**Methylenedioxymethamphetamine (MDMA)**	Concentration (ng/ml)
d-Amphetamin	1,000	3,4-Methylenedioxymethamphetamine HCl (MDMA)	500
d,l-Amphetamine	3,000	3,4-Methylenedioxyamphetamine HCl (MDA)	3,000
l-Amphetamine	50,000	3,4-Methylenedioxyethylamphetamine (MDE)	300
(+/-) 3,4-methylenedioxyamphetamine (MDA)	5,000	**Morphine (MOP)**	
Phentermine	3,000	Morphine	300
d-methamphetamine	>100,000	Codeine	300
l-methamphetamine	>100,000	Ethyl Morphine	300
3,4-Methylenedioxyethylamphetamine(MDE)	100,000	Heroin	300
(+/-)3,4-methylenedioxumethamphetamine (MDMA)	100,000	Hydrocodone	5,000
Barbiturates (BAR)		Hydromorphone	5,000
Secobarbital	300	Morphine-3-β-d-glucuronide	1,000
Amobarbital	300	α -Monoacetylmorphine	400
Alphenol	150	Oxycodone	25,000
Aprobarbital	200	Oxymorphone	10,000
Butabarbital	75	Thebaine	30,000
Butalbital	100	**Opiate (OPI 2000)**	
Butalbital	5,000	Morphine	2,000
Cyclopentobarbital	600	Codeine	2,000
Pentobarbital	5,000	Ethylmorphine	5,000
Phenobarbital	10,000	Heroin	2,000
Benzodiazepine (BZO)		Hydrocodone	12,500
Oxazepam	300	Hydromorphine	5,000
Alprazolam	200	Levorphanol	75,000
α-Hydroxyalprazolam	1,500	α-Monoacetylmorphine	5,000
Benzodiazepine	100	Morphine 3-b-D-glucuronide	2,000
Bromazepam	1,500	β-Monoacetylmorphine	5,000
Chlordiazepam	10,000	Norcodeine	12,500
Chlordiazepoxide	1,500	Normorphone	50,000

Clonazepam HCl	300	Oxycodone	25,000
Clobazam	100	Oxymorphine	25,000
Clonazepam	5,000	Procaine	150,000
Clorazepate dipotassium	200	Thebaine	100,000
Delorazepam	1,500	**Oxycodone(OXY)**	
Desalkylflurazepam	400	Oxycodone	100
Diazepam	200	Dihydrocodeine	50,000
Estazolam	2,500	Codeine	100,000
Flunitrazepam	400	Hydromorphone	100,000
D,L-Lorazepam	1,500	Morphine	>100,000
Midazolam	12,500	Acetylmorphine	>100,000
Nitrazepam	100	Buprenorphine	>100,000
Norchlordiazepoxide	200	Ethylmorphine	>100,000
Nordiazepam	400	**Phenoyclidine (PCP)**	
Temazepam	100	Phencyclidine	25
Triazolam	1,000	4-Hydroxyphencyclidine	12500
Buprenorphine(BUP)		**Trioyclic Antidepressants (TCA)**	
Buprenorphine	10	Nortriptyline	1,000
Buprenorphine -3-D-Glucuronide	15	Nordoxepine	1,000
Norbuprenorphine	20	Trimipramine	3,000
Norbuprenorphine 3-D-Glucuronide	200	Amitriptyline	1,500
Cocaine (COC)		Promazine	1,500
Benzoylecgonine	300	Desipramine	300
Cocaine HCl	750	Imipramine	400
Cocaethylene	12,500	Clomipramine	12,500
Ecgonine	32,000	Doxepine	2,000
Marijuana (THC)		Maprotiline	2,000
11-nor-Δ9-THC-9-COOH	50	Promethazine	25,000
11-nor-Δ8-THC-9-COOH	30	**Methamphetamine (MET)**	
11-hydroxy-Δ9-Tetrahydrocannabinol	2,500	D(+)-Methamphetamine	1,000
Δ8- Tetrahydrocannabinol	7,500	D-Amphetamine	50,000
Δ9- Tetrahydrocannabinol	10,000	Chloroquine	50,000
Cannabinol	100,000	(+/-)-Ephedrine	50,000
Cannabidiol	100,000	(-)-Methamphetamine	25,000
Methadone (MTD)		(+/-)3,4-methylenedioxumethamphetamine(MDMA)	2,000
Methadone	300	β-Phenylethylamine	50,000
Doxylamine	50,000	Trimethobenzamide	10,000
Propoxyphene (PPX)			
d-Norpropoxyphene	300		

pharmaceuticals

LIMITATIONS

1. This test has been developed for testing urine samples only. The performance of this test using other specimens has not been substantiated.
2. Adulterated urine samples may produce erroneous results. Strong oxidizing agents such as bleach (hypochlorite) can oxidize drug analyses. If a sample is suspected of being adulterated, obtain a new sample.
3. This test is a qualitative screening assay. It is not designed to determine the quantitative concentration of drugs or the level of intoxication
4. It is possible that technical or procedural errors, as well as other interfering substances in the urine specimen may cause erroneous results.
5. A negative result may not necessarily indicate drug-free urine. Negative results can be obtained when drug is present but below the cut-off level of the test.
6. The test result does not distinguish between drugs of abuse and certain medicines.
7. A positive result might be obtained from certain foods or food supplements.

MEANING OF SYMBOLS ON PACKAGE


Keep away from sunlight


Store between 4°C-30°C (40°F-86°F)


Keep dry


Do not re-use

Questions?

Any questions, please call us toll-free at **1-855-822-6999**.
Monday – Friday 9:00 a.m.-5:00 p.m. Central Time.
To learn more, please visit us at **www.healthcare-manager.com**
Manufactured for **Easy Healthcare Corporation**
360 Shore Dr. Burr Ridge, IL USA 60527

QUESTIONS AND ANSWERS

The Drug Line is lighter than the Control Line. Does this mean some drug is present?
No. Any line next to the word Drug or the drug abbreviation (depending on the test you have purchased), no matter how dark or light, is considered a Negative Result and no further testing is required. It is possible that the intensity of the lines will vary among the drugs being tested for due to a variety of reasons such as; how diluted the urine is, the pH or protein level of the urine, or interference from a metabolite in the urine that closely resembles the drug.

How soon can I read my results?
Negative result is available to read whenever the Test line which representing the specific drug appears and Control lines shall always appears if test is valid. For positive results you have to wait until 5 minutes when the specific Test line doesn't show up at all while Control lines shall always appears if test is valid.

Are there any factors that can affect the test result?
Certain over-the-counter medications or prescription drugs may cross-react with the Easy@Home Drug Test and cause a Preliminary Positive Result.
The test will only give accurate results on fresh human urine samples. Old or diluted urine samples may not be suitable for testing.
If you are testing someone else, keep in mind that Easy@Home Drug Tests are only as accurate as the urine sample being tested. Samples can easily be "adulterated" (i.e., contaminated or tampered) with common household products such as bleach and other liquids if you're not closely supervising the entire process.
This test provides a screening result only. It is not designed to determine the actual concentration of a drug, the level of intoxication nor is it to be used for legal purposes.

What cut-off levels do Easy@Home Drug Tests use for detecting drugs in urine?
The cut-off level for each drug varies (depending on the type of drug) and is measured in nanogras(ng/ml).
Although Easy@Home Drug Tests are designed to detect a very small amount of a drug in urine, if the amount is below the established cut-off level, you may test negative for that drug even though you may have taken the drug.

How soon after taking a drug can you detect it in urine with a Easy@Home Drug Test and how long can a drug be detected in urine?
Most drugs can be detected in urine with a Easy@Home Drug Test within a few hours after taking the drug; however this can vary depending on the type of drug taken, the amount taken, the frequency of use, and the metabolism of the person being tested.
Each drug is cleared by the body at different rates. Some drugs, for example marijuana, can stay in the body for up to several weeks after use.

If I test negative with a Easy@Home Drug Test, does this guarantee I will test negative on other drug tests administered by a professional?
Many Easy@Home Drug testing products are more than 99 percent accurate in detecting specific drugs according to the designated cut-off levels. However, if a more sensitive test is administered, there is a chance of testing positive if drugs are present in urine.

pharmaceuticals

Zachary Prensky, CEO	Signature	Date