TINSAL-T2D Stage 2 Form BP24HR
24 Hour Blood Pressure Monitoring

BPVISID

BAS=Visit 3
W24=Visit 9
W48=Visit 11

Clinic ☐☐ Participant ID ☐☐☐☐☐ Visit ID ☐☐☐

CLINIC PATIENT

1. Nickname ☐☐☐☐☐☐ BPNICKNA

2. Staff ID ☐☐☐ BPSTAFF

3. Date and time BP Monitor turned ON (mm/dd/yyyy)

Date: ☐☐/☐☐/☐☐☐☐ BPONDATE

BPONTIME Time: ☐☐:☐☐ ☐1 AM ☐2 PM BPONAMPM

4. Date and time BP Monitor turned OFF (mm/dd/yyyy)

Date: ☐☐/☐☐/☐☐☐☐ BPOFFDAT

BPOFFTIM Time: ☐☐:☐☐ ☐1 AM ☐2 PM BPOFFAMP

5. Was the monitoring successfully completed? ☐1 Yes ☐2 No BPSUCCES

If NO, why not? BPSUCCY _____

Instructions: Fill out each time participant successfully monitors blood pressure for 24 hours. If monitoring was not successfully completed fill out the top portion and stop. Results should come from monitor's software or be noted as calculated in a comment.

A. 24 hour Blood Pressure Readings

		Systolic / Diastolic
6. 24 hour mean	BP24MES	☐☐☐/☐☐☐ BP24MED mmHg
7. Standard Deviation	BP24SYS	☐☐.☐☐/☐☐.☐☐ BP24SDD
8. Number of Readings	BP24NUM	☐☐☐
a. Peak BP reading	BP24PSYS	☐☐☐/☐☐☐ BP24PDIA mmHg
b. Trough BP reading	BP24TSYS	☐☐☐/☐☐☐ BP24TDIA mmHg
9. Mean Heart Rate	BP24HR	☐☐☐ bpm
10. Mean Pulse Pressure	BP24PP	☐☐☐ mmHg
11. Mean Arterial Pressure (MAP)	BP24MAP	☐☐☐ mmHg

B. Daytime Blood Pressure Readings

		Systolic / Diastolic
12. Mean	BPDAYMES	___ / ___ BPDAYMED mmHg
13. Standard Deviation	BPDAYSDS	___.___ / ___.___ BPDAYSDD
14. Number of Readings	BPDAYNUM	___
a. Peak BP reading	BPDYPSYS	___ / ___ BPDYPDIA mmHg
b. Trough BP reading	BPDYTSYS2	___ / ___ BPDYTDIA mmHg
15. Mean Heart Rate	BPDAYHR	___ bpm
16. Mean Arterial Pressure (MAP)	BPDAYPP	___ mmHg

C. Nocturnal Blood Pressure Readings

		Systolic / Diastolic
17. Mean	BPNCMSY	___ / ___ BPNCMDI mmHg
18. Standard Deviation	BPNOCSDS	___.___ / ___.___ BPNOCSDD
19. Number of Readings	BPNOCNUM	___
a. Peak BP reading	BPNCPKSY	___ / ___ BPNCPKDI mmHg
b. Trough BP reading	BPNCTRSY	___ / ___ BPNCTRDI mmHg
20. Mean Heart Rate	BPNOCHR	___ bpm
21. Mean Arterial Pressure (MAP)	BPNOCPP	___ mmHg

TINSAL-T2D Stage 2 Form BP24HR
24 Hour Blood Pressure Monitoring

Clinic	Participant ID	Visit ID
☐☐	☐☐☐☐☐	☐☐☐

BAS=Visit 3
W24=Visit 9
W48=Visit 11

D. 24 Hour Urine Collection

22. Was urine collected at this visit? BPURINE ☐1 Yes ☐2 No

23. Total volume of urine collected over 24 hour period: ☐☐☐☐ mL BPURVOL

24. Time of start of collection: BPURSTAR ☐☐ : ☐☐ ☐1 AM ☐2 PM BPURSTAM

25. Time of end of collection: BPURSTOP ☐☐ : ☐☐ ☐1 AM ☐2 PM BPURSPAM

TINSAL T2D Stage 2 Form CONMED
Concomitant Medication Log

Clinic CLINIC | Participant ID PATIENT | CMPAGENO | Page No. ⇐

If this is the first time a log entry has been made for this participant, enter 01. If this page is an addition to a log that already exists, enter the next sequential page number.

Nickname CMNICKNA

Instructions: At the screening visit, list all concomitant medications that the participant is currently taking. At all other visits, update this log with all concomitant medications that the participant has taken since the previous visit, or is currently taking.

A. Concomitant Medications

	Category (a)	Start Date OR Date of change in dose or frequency (mm/dd/yyyy)	End Date OR Last date at this dose and frequency (mm/dd/yyyy)	Dose	Unit	Route (a)
1.	CMCATEG1	/ / CMSTADT1	/ / CMENDDT1	CMDOSE1 .	CMUNIT1	CMROUTE1
	Medication:	CMMEDIC1				
CMFREQ1	Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h ☐7 Other (specify):	CMFREQS1				
2.	CMCATEG2	/ / CMSTADT2	/ / CMENDDT2	CMDOSE2 .	CMUNIT2	CMROUTE2
	Medication:	CMMEDIC2				
CMFREQ2	Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h ☐7 Other (specify):	CMFREQS2				
3	CMCATEG3	/ / CMSTADT3	/ / CMENDDT3	CMDOSE3	CMUNIT3	CMROUTE3
	Medication:	CMMEDIC3				
CMFREQ3	Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h ☐7 Other (specify):	CMFREQS3				

(a) For Category and Route codes, refer to the lists on the next page.

TINSAL-T2D Stage 2 Form CONMED
Concomitant Medications

Medication	Category
Antihypertensive agents (Loop diuretics, thiazide diuretics, K-sparing diuretic agents, potassium supplements, ARBs, ACE inhibitors, dihydropyridine calcium channel blockers, non-dihydropyridine calcium channel blockers, peripheral alpha-blockers, central alpha-adrenergic agonists, beta-blockers, vasodilators, reserpine, etc.)	01
Cardiovascular drugs (digitalis, anti-arrhythmics, nitrates, etc.)	02
Lipid-lowering drugs (Bile acid sequestrants, HMG CoA reductase inhibitors (statins), fibrates, cholesterol absorption inhibitors, niacin, nicotinic acid, etc.)	03
Oral anticoagulants (warfarin, coumadin, etc). **This is an exclusionary medication. If the participant has not been randomized, discontinue his or her participation in the study. If this is a follow-up visit, STOP study medication. Fill out MEDLOG.**	04
Heparins. **This is an exclusionary medication. If the participant has not been randomized, discontinue his or her participation in the study. If this is a follow-up visit, STOP study medication. Fill out MEDLOG.**	05
Inhibitors of platelet aggregation (except aspirin)	06
Cox-2 inhibitor	07
Aspirin	08
Progestins	09
Estrogens (excluding vaginal creams)	10
Thyroid agents	11
Oral asthma drugs (except steroids)	12
Inhaled steroids for asthma	13

Medication	Category
Antidepressant	14
Antipsychotic	15
Erectile dysfunction drugs	16
Weight loss drug	17
Steroids	18
Any other prescribed medication	19
Vitamins and/or nutritional supplements	20
Over-the-counter medications	21
Herbal/alternative therapies	22

Route	Code
Intravenous	IV
Intramuscular	IM
By mouth	PO
Subcutaneous	SC
Other	OTH
Vagina	PV
Each eye	OU
Rectal	PR
Sublingual	SL
Inhaled	INH
Topical	TOP
Left eye	OD
Right eye	OD

TINSAL-T2D Stage 2 Log of CONSENT
Informed Consent Permissions

Clinic CLINIC | Participant ID PATIENT | Date of Form CONSENT completion (mm/dd/yyyy) CNVISIDT

1. Nickname CNNICKNA
2. Staff ID CNSTAFFI

Instructions: Indicate which permissions have been given by the participant on his or her informed consent.

Genetic Study Permissions

3. Participant gives permission for his or her DNA and RNA to be collected. ☐1 Yes ☐2 No CNDNARNA

4. Participant gives permission for researchers to make a living line for study. ☐1 Yes ☐2 No CNLIVING

5. Participant gives permission for his or her samples to be sent to the NIDDK Central Repositories. ☐1 Yes ☐2 No CNNIDDK

(Applicable to the University of Nebraska VA Medical Center only.)

Check one of the following:

CNVAMED

☐1 Participant agrees to allow his or her genetic sample to be studied for genes related to any major disease or health condition or risk factor.

☐2 Participant agrees to allow his or her genetic sample to be studied only for genes related to diabetes, obesity, inflammation, blood pressure, blood cholesterol abnormalities, heart disease, or other risk factors for heart disease or for diabetes or complications of diabetes.

☐3 Participant agrees to allow his or her genetic samples to be used only for this study.

☐4 Participant declines permission to collect his or her DNA and RNA for a genetic sample.

Sub-Study Permissions *(Applicable to participating sites only.)*

6. Participant gives permission to participate in FMD (Flow Mediated Vasodilation) study ☐1 Yes ☐2 No CNFMD

7. Participant gives permission to participate in 24 hour blood pressure monitoring AND to collect 24 hour urine samples ☐1 Yes ☐2 No CN24HR

8. Date of participant's signature (mm/dd/yyyy) ☐☐/☐☐/☐☐☐☐ CNSIGNDT

TINSAL-T2D Stage 2 Form EXERCISE
Exercise Questionnaire

EXVISITI

Clinic	Participant ID	Visit ID
CLINIC	PATIENT	

BAS=Visit 3
W14=Visit 7
W26=Visit 9

Nickname	EXNICKNA	
Visit date (mm/dd/yyyy)	EXVISITD	/ /
Staff ID	EXSTAFFI	

Instructions: The participant completes this form during Visit 3 (baseline), and during Visit 7 (Stage 1) or Visit 9 (Stage 2)

1. Which category best describes your main occupation? (check only one) EXOCCUPA

- ☐ 1 Clerical work, driving, shopkeeping, teaching, studying, housework, medical practice, any occupation requiring a university education
- ☐ 2 Factory work, plumbing, carpentry, farming (not requiring a university education)
- ☐ 3 Dock work, construction work, sports (not requiring a university education)

2. How often do you sit at work? EXSIT

- ☐ 1 Never
- ☐ 2 Seldom
- ☐ 3 Sometimes
- ☐ 4 Often
- ☐ 5 Always

3. How often do you stand at work? EXSTAND

- ☐ 1 Never
- ☐ 2 Seldom
- ☐ 3 Sometimes
- ☐ 4 Often
- ☐ 5 Always

4. How often do you walk at work? EXWALKW

- ☐ 1 Never
- ☐ 2 Seldom
- ☐ 3 Sometimes
- ☐ 4 Often
- ☐ 5 Always

5. How often do you lift heavy loads at work?

EXLIFT

- ☐ 1 Never
- ☐ 2 Seldom
- ☐ 3 Sometimes
- ☐ 4 Often
- ☐ 5 Very often

6. How often are you tired after working?

EXTIRED

- ☐ 1 Very often
- ☐ 2 Often
- ☐ 3 Sometimes
- ☐ 4 Seldom
- ☐ 5 Never

7. How often do you sweat at work?

EXSWEATW

- ☐ 1 Very often
- ☐ 2 Often
- ☐ 3 Sometimes
- ☐ 4 Seldom
- ☐ 5 Never

8. In comparison with others of your own age, how much heavier or lighter do you think your work is?

EXHEAVIE

- ☐ 1 Much heavier
- ☐ 2 Heavier
- ☐ 3 As heavy
- ☐ 4 Lighter
- ☐ 5 Much lighter

9. Do you play sports? EXSPORT1 ☐ 1 Yes ☐ 2 No

If YES,

a. Which category best describes the sport you play most frequently? (check only one)

EXSPOR1

- ☐ 1 Billiards, sailing, bowling, golf
- ☐ 2 Badminton, cycling, dancing, swimming, tennis
- ☐ 3 Boxing, basketball, football, rugby, rowing, soccer

b. How many hours per week?

EXSPORH1

- ☐ 1 Less than 1 hour
- ☐ 2 Between 1 and 2 hours
- ☐ 3 Between 2 and 3 hours
- ☐ 4 Between 3 and 4 hours
- ☐ 5 More than 4 hours

c. How many months per year?

EXSPORM1

- ☐ 1 Less than 1 month
- ☐ 2 Between 1 and 3 months
- ☐ 3 Between 4 and 6 months
- ☐ 4 Between 7 and 9 months
- ☐ 5 More than 9 months

d. Do you play a second sport?

EXSPORT2

- ☐ 1 Yes
- ☐ 2 No

If YES,

i. Which category best describes the sport? (check only one)

EXSPORC2

- ☐ 1 Billiards, sailing, bowling, golf
- ☐ 2 Badminton, cycling, dancing, swimming, tennis
- ☐ 3 Boxing, basketball, football, rugby, rowing, soccer

ii. How many hours per week?

EXSPORH2

- ☐ 1 Less than 1 hour
- ☐ 2 Between 1 and 2 hours
- ☐ 3 Between 2 and 3 hours
- ☐ 4 Between 3 and 4 hours
- ☐ 5 More than 4 hours

iii. How many months per year?

EXSPORM2

- ☐ 1 Less than 1 month
- ☐ 2 Between 1 and 3 months
- ☐ 3 Between 4 and 6 months
- ☐ 4 Between 7 and 9 months
- ☐ 5 More than 9 months

10. How do you think your physical activity during leisure time compares to others of your own age?

EXACTIVI

- ☐ 1 Much more
- ☐ 2 More
- ☐ 3 The same
- ☐ 4 Less
- ☐ 5 Much less

11. How often do you sweat during leisure time?

EXSWEATL

- ☐ 1 Very often
- ☐ 2 Often
- ☐ 3 Sometimes
- ☐ 4 Seldom
- ☐ 5 Never

12. How often do you play sports during leisure time?

EXSPORTL

- ☐ 1 Very often
- ☐ 2 Often
- ☐ 3 Sometimes
- ☐ 4 Seldom
- ☐ 5 Never

13. How often do you watch television or use a computer during leisure time?

EXWATCH

- ☐ 1 Very often
- ☐ 2 Often
- ☐ 3 Sometimes
- ☐ 4 Seldom
- ☐ 5 Never

14. How often do you walk during leisure time?

EXWALKL

- ☐ 1 Very often
- ☐ 2 Often
- ☐ 3 Sometimes
- ☐ 4 Seldom
- ☐ 5 Never

15. How often do you cycle during leisure time?

EXCYCLE

- ☐ 1 Very often
- ☐ 2 Often
- ☐ 3 Sometimes
- ☐ 4 Seldom
- ☐ 5 Never

16. How many minutes do you walk and/or cycle per day to and from work, school or shopping?

EXWALKDY

- ☐ 1 Less than 5 minutes
- ☐ 2 Between 5 and 15 minutes
- ☐ 3 Between 15 and 30 minutes
- ☐ 4 Between 30 and 45 minutes
- ☐ 5 More than 45 minutes

FMD [V1]: Vascular Function Analysis Form
(TINSAL-T2D Substudy)

Clinic: CLINIC Participant ID: PATIENT

Visit ID: FMDVISID Visit Date: FMDVISDT

	Max Velocity	% Max Velocity Change	Integral Velocity	% Integral Velocity	Diameter	% Vasodilation	Blood Pressure Systolic	Blood Pressure Diastolic	Heart Rate
Baseline	VELOCITY1		INTVELO1		DIAMETER1		BPSYS1	BPDIA1	HEARTRAT1
Reactive Hyperemia	VELOCITY2	VELOCHAN2	INTVELO2	INTVELP2	DIAMETER2	VASODILA2	BPSYS2	BPDIA2	HEARTRAT2
Pre-TNG	VELOCITY3		INTVELO3		DIAMETER3		BPSYS3	BPDIA3	HEARTRAT3
TNG	VELOCITY4	VELOCHAN4	INTVELO4	INTVELP4	DIAMETER4	VASODILA4	BPSYS4	BPDIA4	HEARTRAT4

Comments:

FMDCOMM1

FMDCOMM2

TINSAL-T2D Stage 2 Form Health History and ROS FORM A
Health History and Review of Systems

HHVISIT

Clinic (CLINIC) | Participant ID (PATIENT) | Visit ID | SCR=Visit 1

1. Nickname (HHNICKNA)
2. Staff ID (HHSTAFF)

A. Medical and Health History

Instructions:

Fill out FORM A at participant's first visit (screening) and update this form only as needed:

If this is the participant's first visit, *check all conditions with which the participant has ever been diagnosed by a health care provider. If the participant has been diagnosed with the condition more than once, enter the date of the first diagnosis and the end date of the last episode.*

If this is not the participant's first visit:
(a) Review this Health History and ROS Form A. .Ask the participant about conditions that were marked as continuing. If the condition has resolved, enter the end date below and complete the Relationship to Drug, Action Taken, Severity, Outcome and Treatment columns using the "Reference Marks and Codes" from the last page of this form .

(b)Check all conditions with which a health care provider has diagnosed the participant since the previous visit. For these conditions, enter the date of diagnosis. Also, enter the end date, or check the "check here if continuing" box.

(a) – (f) Refer to the end of this form for explanation of reference marks and codes.

TINSAL-T2D Stage 2 Form Health History and ROS FORM A
Health History and Review of Systems

Clinic | Participant ID | Visit ID

A. Medical and Health History

Check all that apply ⇓	Date of onset (a)	End date (a) OR check here if continuing ⇓	Relationship to Drug (b) ⇓	Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
3. Eyes, ears, nose and throat			Note: for these vars, combine the prefix of the condition with the following numeric suffix				
HHARETI1 a. Retinopathy requiring laser treatment ☐	/ / HHRETI2	/ HHARETI3	4 5	6	7	8	9
b. Other HHAEYEO1 ☐	/ / HHAEYEO2	/ HHAEYEO3	4 5	6	7	8	9
4. Respiratory HHARESP1 ☐	/ / HHARESP2	HHARESP3	4 5	6	7	8	9
5. Cardiovascular HHAHIGH1							
a. High blood pressure ☐	/ / HHAHIGH2	/ HHAHIGH3	4 5	6	7	8	9
b. High LDL (>140 mg/dL) HHAHLDL1 ☐	/ / HHAHLDL2	/ HHAHLDL3	4 5	6	7	8	9
c. High triglycerides (>150 mg/dL) HHAHTRI1 ☐	/ / HHAHTRI2	/ HHAHTRI3	4 5	6	7	8	9
d. Low HDL (males: <40; females: <50 mg/dL) HHALHDL1 ☐	/ / HHALHDL2	/ HHALHDL3	4 5	6	7	8	9
e. MI HHAMI1 ☐	/ / HHAMI2	/ HHAMI3	4 5	6	7	8	9
f. Angina HHAANGI1 ☐	/ / HHAANGI2	/ HHAANGI3	4 5	6	7	8	9

(a) – (f) Refer to the end of this form for explanation of reference marks and codes.

Clinic | Participant ID | Visit ID

A. Medical and Health History (continued)

Check all that apply	Date of onset (a)	End date (a) OR check here if continuing	Relationship to Drug (b)	Action Taken (c)	Severity (d)	Outcome (e)	Treatment (f)
g. CABG/PTCA HHACABG1	HHACABG2	HHACABG3	4	5	6	7	8	9
h. Other HHACARO1 ☐	HHACARO2	HHACARO3	HHACAR4 5	6	7	8	9
6. Gastrointestinal HHAUPPE1							
a. Upper GI bleed ☐	HHAUPPE2	HHAUPPE3	HAUPPE4 HAUPPE5	HAUPPE6	HAUPPE7	HAUPPE8	HHAUPPE9
b. Lower GI bleed HHALOWE1	HHALOWE2	HHALOWE3	4	5	6	7	8	9
c. Other HHAGASO1 ☐	HHAGASO2	HHAGASO3	4	5	6	7	8	9
7. Musculoskeletal HHAMUSC1	HHAMUSC2	HHAMUSC3	4	5	6	7	8	9
8. Neurological							
a. Peripheral neuropathy HHAPERI1	HHAPERI2	HHAPERI3	4	5	6	7	8	9
b. Autonomic neuropathy HHAAUTO1	HHAAUTO2	HHAAUTO3	4	5	6	7	8	9
c. Other HHANEUO1 ☐	HHANEUO2	HHANEUO3	4	5	6	7	8	9

(a) – (f) Refer to the end of this form for explanation of reference marks and codes.

Clinic | Participant ID | Visit ID

A. Medical and Health History (continued)

Check all that apply	Date of onset (a)	End date (a) OR check here if continuing		Relationship to Drug (b) Action Taken (c)	Severity (d)	Outcome (e)	Treatment (f)
9. Endocrine (other than diabetes)	HHAENDO1 / / HHAENDO2	/ HHAENDO3	4	5	6	7	8	9
10. Hematopoietic / lymphatic	HHAHEMA1 / / HHAHEMA2	/ HHAHEMA3	4	5	6	7	8	9
11. Dermatologic	☐ HHADERM1 / / HHADERM2	/ HHADERM3	4	5	6	7	8	9
12. Psychological								
a. Depression requiring hospitalization	HHADEPR1 / / HHADEPR2	/ HHADEPR3	4	5	6	7	8	9
b. Other HHAPSYO1	☐ / / HHAPSYO2	/ HHAPSYO3	4	5	6	7	8	9
13. Genitourinary								
a. Proteinuria HHAPROT1	/ / HHAPROT2	/ HHAPROT3	4	5	6	7	8	9
b. Other HHAGENO1	☐ / / HHAGENO2	/ HHAGENO3	4	5	6	7	8	9

(a) – (f) Refer to the end of this form for explanation of reference marks and codes.

Clinic | Participant ID | Visit ID

A. Medical and Health History (continued)

Check all that apply ⇓	Date of onset (a)	End date (a) OR check here if continuing ⇓		Relationship to Drug (b) ⇓	Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
14. Other								
a. Specify diagnosis #1	HHDIAG11							
	/ / HHDIAG12	/ / HHDIAG13	14	15	16	17	18	19
b. Specify diagnosis #2	HHDIAG21							
	/ / HHDIAG22	/ / HHDIAG23	24	25	26	27	28	29
c. Specify diagnosis #3	HHDIAG31							
	/ / HHDIAG32	/ / HHADIAG33	34	35	36	37	38	39

(a) – (f) Refer to the end of this form for explanation of reference marks and codes.

Clinic	Participant ID	Visit ID	SCR=Visit 1
☐☐	☐☐☐☐☐	☐☐☐	

Reference Marks and Codes:

(a) Dates: Enter date in mm/dd/yyyy format. Enter 06 for month if unknown. Enter 15 for day if unknown. Do not enter date of diagnosis or onset for conditions or symptoms previously reported.

(b) Relationship to Drug: To be completed for baseline and follow-up visits only.
1-Definite
2-Probable
3-Possible
4-Unlikely
5-Unrelated

(c) Action taken: To be completed for baseline and follow-up visits only.
1-None
2-Discontinued
3-Reduced
4-Interrupted

(d) Severity: To be completed for baseline and follow-up visits only.
1- Mild: awareness of symptom but easily tolerated
2- Moderate: discomfort enough to cause interference with usual activity
3- Severe: incapacitating with inability to work or do usual activity

(e) Outcome: To be completed for baseline and follow-up visits only.
1-Recovered
2-Resolved, but sequelae / residual effect(s) remain
3-Still present
4-Death

(f)Treatment: To be completed for baseline and follow-up visits only.
1-None
2-Medication required; no hospitalization
3-Hospitalization required or prolonged; no medication required
4-Medication required; hospitalization required or prolonged
5-Other

TINSAL-T2D Stage 2 Form Health History and ROS FORM B
Health History and Review of Systems

HH2VISIT

Clinic | **Participant ID** | **Visit ID**

SCR – Visit 1 **W12 – Visit 7**
RUN – Visit 2 **W16 – Visit 8**
BAS – Visit 3 **W24 – Visit 9**
W02 – Visit 4 **W36 – Visit 10**
W04 – Visit 5 **W48 – Visit 11**
W08 – Visit 6 **W50 – Visit 12**

CLINIC PATIENT

1. Nickname HHNICKNA
2. Staff ID HHSTAFF

B. Interim History / Review of Symptoms

Instructions:

Form B needs to be completed at every visit.

At the screening visit, *all conditions that the participant has experienced within the past 6 months are recorded.*

At subsequent visits, *review Form B from the* previous *visit and ask the subject if any of the previously entered conditions have resolved or if they are continuing. In addition, be sure to ask if there have been any new conditions. Complete a* <u>new</u> *Form B by adding any new conditions that have been experienced since the previous visit, adding whether previous conditions are continuing, and adding if any of the previous conditions have resolved. If any of the previous conditions from the last visit are still continuing, mark the condition "continuing" on the* <u>new</u> *Form B. If a condition has been resolved then on the* <u>new</u> *Form B, record the date of resolution. If the visit is BAS or later, complete "action taken", "severity", "outcome", and "treatment" sections using the codes found at the end of the form for all symptoms resolved or continuing.*

TINSAL-T2D Stage 2 Form Health History and ROS FORM B
Health History and Review of Systems

Clinic | Participant ID | Visit ID

SCR – Visit 1 | W12 – Visit 7
RUN – Visit 2 | W16 – Visit 8
BAS – Visit 3 | W24 – Visit 9
W02 – Visit 4 | W36 – Visit 10
W04 – Visit 5 | W48 – Visit 11
W08 – Visit 6 | W50 – Visit 12

B. Interim History / Review of Symptoms

Check all that apply	Date of onset (a)	End date (a) OR check here if continuing		Relationship to Drug (b)	Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
3. Eyes								
a. Blurry vision HHBLURR1	HHBLURR2	HHBLURR3	4	5	6	7	8	9
b. Loss of vision HHLOSSO1	HHLOSSO2	HHLOSSO3	4	5	6	7	8	9
c. Dots / flashes HHDOTSF1	HHDOTSF2	HHDOTSF3	4	5	6	7	8	9
d. Other HHBEYEO1	HHBEYEO2	HHBEYEO3	4	5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBEYEOS								
4. Ears								
a. Earaches HHBEARA1	HHBEARA2	HHBEARA3	4	5	6	7	8	9
b. Infections HHBINFE1	HHBINFE2	HHBINFE3	4	5	6	7	8	9
c. Ringing in the ears HHBRING1	HHBRING2	HHBRING3	4	5	6	7	8	9
d. Other HHBEARO1	HHBEARO2	HHBEAR03	4	5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBEAROS								

Clinic | Participant ID | Visit ID

SCR – Visit 1 | W12 – Visit 7
RUN – Visit 2 | W16 – Visit 8
BAS – Visit 3 | W24 – Visit 9
W02 – Visit 4 | W36 – Visit 10
W04 – Visit 5 | W48 – Visit 11
W08 – Visit 6 | W50 – Visit 12

B. Interim History / Review of Symptoms (continued)

Check all that apply ⇓	Date of onset (a)	End date (a) OR check here if continuing ⇓	⇓	Relationship to Drug (b) Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
5. Nose / sinuses							
a. Frequent colds HHBREQ1	/ / HHBREQ2	/ / HHBFREQ3	4	5	6	7	8	9
b. Stuffiness HHBSTUF1	/ / HHBSTUF2	/ / HHBSTUF3	4	5	6	7	8	9
c. Nose bleeds HHBNOSE1	/ / HHBNOSE2	/ / HHBNOSE3	4	5	6	7	8	9
d. Runny nose HHBRUNN1	/ / HHBRUNN2	/ / HHBRUNN3	4	5	6	7	8	9
e. Other HHBNOSO1	/ / HHBNOSO2	/ / HHBNOSO3	4	NNBNOSO5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary)	HHBNOSOS							
6. Mouth / throat							
a. Mouth sores HHBMOUS1	/ / HHBMOUS2	/ / HHBMOUS3	4	5	6	7	8	9
b. Hoarseness HHBHOAR1	/ / HHBHOAR2	/ / HHBHOAR3	4	5	6	7	8	9
c. Bleeding gums HHBBLEE1	/ / HHBBLEE2	/ / HHBBLEE3	4	5	6	7	8	9
d. Other HHBBMOUO1	/ / HHBMOUO2	/ / HHBMOUO3	4	5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary)	HHBMOUOS							

Clinic ☐☐ Participant ID ☐☐☐☐☐ Visit ID ☐☐☐

SCR – Visit 1 W12 – Visit 7
RUN – Visit 2 W16 – Visit 8
BAS – Visit 3 W24 – Visit 9
W02 – Visit 4 W36 – Visit 10
W04 – Visit 5 W48 – Visit 11
W08 – Visit 6 W50 – Visit 12

B. Interim History / Review of Symptoms (continued)

Check all that apply ⇓	Date of onset (a)	End date (a) OR check here if continuing ⇓	⇓	Relationship to Drug (b) Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
7. Neck				HHPNECP6		HHPNECP8	
a. Pain or stiffness HHBNECP1	HHBNECP2	HHBNECP3	4 HHPNECP5		HHPNECP7		HHPNECP9
b. Swollen glands HHBSWOL1	HHBSWOL2	HHBSWOL3	4	5 6	7	8	9
c. Other HHBNECO1 ☐	HHBNECO2	HHBNECO3	4	5 6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBNECOS							
8. If female							
a. Change in cycle HHBCHAN1	HHBCHAN2	HHBCHAN3	4	5 6	7	8	9
b. Other HHBFEMO1 ☐	HHBFEMO2	HHBFEMO3	4	5 6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBFEMOS							
9. Breasts							
a. Lumps HHBLUMP1 ☐	HHBLUMP2	HHBLUMP3	4	5 6	7	8	9
b. Nipple discharge HHBNIPP1	HHBNIPP2	HHBNIPP3	4	5 6	7	8	9
c. Other HHBBREO1 ☐	HHBBREO2	HHBBREO3	4	5 6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBBREOS							

TINSAL-T2D Stage 2 Form Health History and ROS FORM B
Health History and Review of Systems

Clinic | Participant ID | Visit ID

SCR – Visit 1 | RUN – Visit 2 | BAS – Visit 3 | W02 – Visit 4 | W04 – Visit 5 | W08 – Visit 6 | W12 – Visit 7 | W16 – Visit 8 | W24 – Visit 9 | W36 – Visit 10 | W48 – Visit 11 | W50 – Visit 12

B. Interim History / Review of Symptoms (continued)

Check all that apply	Date of onset (a)	End date (a) OR check here if continuing	Relationship to Drug (b)	Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
10. Respiratory							
a. Frequent cough HHBFREC1	HHBFREC2	HHBFREC3	4 5	6	7	8	9
b. Asthma HHBASTH1	HHBASTH2	HHBASTH3	4 5	6	7	8	9
c. Shortness of breath with exercise HHBSHOE1	HHBSHOE2	HHBSHOE3	4 HHBSHO5 6		HHSHOE7	8	9
d. Shortness of breath at rest HHBSHOR1	HHBSHOR2	HHBSHOR3	4 5	6	7	8	9
e. Other HHBRESO1	HHBRESO2	HHBRESO3	4 5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary)		HHBRESOS					
11. Cardiac							
a. Palpitations (irregular heart beats) HHBPALP1	HHBPALP2	HHBPALP3	4 5	6	7	8	9
b. Chest pain or discomfort HHBCHES1	HHBCHES2	HHBCHES3	4 5	6	7	8	9
c. Trouble breathing at night HHBTROU1	HHBTROU2	HHBTROU3	4 5	6	7	8	9
d. Swelling in legs or feet HHBSWEL1	HHBSWEL2	HHBSWEL3	4 5	6	7	8	9

B. Interim History / Review of Symptoms (continued)

Check all that apply	Date of onset (a)	End date (a) OR check here if continuing	Relationship to Drug (b)	Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
e. Other HHBCARO1	HHBCARO2	HHBCAR03	4	5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBCAROS								
12. Gastrointestinal								
a. Heartburn HHBHEAR1	HHBHEAR2	HHBHEAR3	4	5	6	7	8	9
b. Trouble swallowing HHBTROS1	HHTROS2	HHBTROS3	4	5	6	7	8	9
c. Nausea HHBNAUS1	HHBNAUS2	HHBNAUS3	4	5	6	7	8	HHBAUS9
d. Vomiting HHBVOMI1	HHBVOMI2	HHBVOMI3	4	5	6	7	8	9
e. Diarrhea HHBDIAR1	HHBDIAR2	HHBDIAR3	4	HHBIAR5	6	7	8	9
f. Bloody stools HHBBLOO1	HHBBLOO2	HHBBLOO3	4	5	6	7	8	9
g. Constipation HHBCONS1	HHBCONS2	HHBCONS3	4	5	6	7	8	9
h. Hemorrhoids HHBHEMO1	HHBHEMO2	HHBHEMO3	4	5	6	HHBHEOM7	8	9
i. Excessive thirst or hunger HHBEXCE1	HHBEXCE2	HHBEXCE3	4	5	6	7	8	9
j. Dark tarry stools HHBDARK1	HHBDARK2	HHBDARK3	HHBDARK4	5	6	7	8	9

Clinic | Participant ID | Visit ID

SCR – Visit 1 | RUN – Visit 2 | BAS – Visit 3 | W02 – Visit 4 | W04 – Visit 5 | W08 – Visit 6 | W12 – Visit 7 | W16 – Visit 8 | W24 – Visit 9 | W36 – Visit 10 | W48 – Visit 11 | W50 – Visit 12

B. Interim History / Review of Symptoms (continued)

Check all that apply	Date of onset (a)	End date (a) OR check here if continuing	Relationship to Drug (b)	Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
k. Change in bowel habit HHBCHAG1	HHBCHAG2	HHBCHAG3	4	5	6	7	8	9
l. Other HHBGASO1	HHBGASO2	HHBGASO3	4	5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBGASOS								
13. Urinary								
a. Excessive frequency HHBEXCF1	HHBEXCF2	HHBEXCF3	4	5	6	7	8	9
b. Bloody urine HHBBLOY1	HHBBLOY2	HHBBLOY3	4	5	6	7	8	9
c. Burning or pain on urination HHBBURN1	HHBBURN2	HHBBURN3	4	5	6	7	8	9
d. Urgency HHBURGE1	HHBURGE2	HHBURGE3	4	5	6	7	8	9
e. Incontinence HHBINCO1	HHBINCO2	HHBINCO3	4	5	6	7	8	9
f. Infections HHBINFC1	HHBINFC2	HHBINFC3	4	5	6	7	8	9
g. Waking at night to urinate HHBWAKE1	HHBWAKE2	HHBWAKE3	4	5	6	7	8	9
h. Other HHBURIO1	HHBURIO2	HHBURIO3	4	5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBURIOS								

Clinic | Participant ID | Visit ID

SCR – Visit 1 | RUN – Visit 2 | BAS – Visit 3 | W02 – Visit 4 | W04 – Visit 5 | W08 – Visit 6 | W12 – Visit 7 | W16 – Visit 8 | W24 – Visit 9 | W36 – Visit 10 | W48 – Visit 11 | W50 – Visit 12

B. Interim History / Review of Symptoms (continued)

Check all that apply	Date of onset (a)	End date (a) OR check here if continuing	Relationship to Drug (b)	Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
14. Musculoskeletal							
a. Stiffness HHBSTIF1	/ / HHBSTIF2	/ / HHBSTIF3	4 5	6	7	8	9
b. Muscle or joint pains HHBMUSC1	/ / HHBMUSC2	/ / HHBMUSC3	4 5	6	7	8	9
c. Arthritis HHBARTH1	/ / HHBARTH2	/ / HHBARTH3	4 5	6	7	8	9
d. Backache HHBBACK1	/ / HHBBACK2	/ / HHBBACK3	4 5	6	7	8	9
e. Other HHBMUSO1	/ / HHBMUSO2	/ / HHBMUSO3	4 5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary)	HHBUSOS						
15. Neurological							
a. Fainting / blackouts HHBFAIN1	/ / HHBFAIN2	/ / HHBFAIN3	4 5	6	7	8	9
b. Numbness or tingling HHBNUMB1	/ / HHBNUMB2	/ / HHBNUMB3	4 5	6	7 HHBNUM8		HHBNUM9
c. Seizures HHBSEIZ1	/ / HHBSEIZ2	/ / HHBSEIZ3	4 5	6	7	8	9
d. Hand tremors HHBHAND1	/ / HHBHAND2	/ / HHBHAND3	4 5	6	7	8	9
e. Nervousness HHBNERV1	/ / HHBNERV2	/ / HHBNERV2	4 5	6	7	8	9

Clinic | Participant ID | Visit ID

SCR – Visit 1 | RUN – Visit 2 | BAS – Visit 3 | W02 – Visit 4 | W04 – Visit 5 | W08 – Visit 6 | W12 – Visit 7 | W16 – Visit 8 | W24 – Visit 9 | W36 – Visit 10 | W48 – Visit 11 | W50 – Visit 12

B. Interim History / Review of Symptoms (continued)

Check all that apply	Date of onset (a)	End date (a) OR check here if continuing	Relationship to Drug (b)	Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)
f. Depression HHBDEPR1	HHBDEPR2	HHBDEPR3	4	HHPDEPR5	HHPDEPR7		HHPDEPR9
				HHPDEPR6		HHPDEPR8	
g. Other HHBNEUO1	HHBNEUO2	HHBNEUO3	4	5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBNEUOS								
16. Hematologic								
a. Easy bruising or bleeding HHBEASY1	HHBEASY2	HHBEASY3	4	5	6	7	8	9
b. Other HHBHEAO1	HHBHEAO2	HHBHEAO3	4	5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBHEAOS								
17. General								
a. Dizzy HHBDIZZ1	HHBDIZZ2	HHBDIZZ3	4	5	6	7	8	9
b. Weakness or fatigue HHBWEAK1	HHBWEAK2	HHBWEAK3	4	5	6	7	8	9
c. Rashes HHBRASH1	HHBRASH2	HHBRASH3	4	5	6	7	8	9
d. Other HHBGEN01	HHBGEN02	HHBGENO3	4	5	6	7	8	9
Specify (list additional symptoms in Question 18 if necessary) HHBGENOS								

B. Interim History / Review of Symptoms (continued)

Check all that apply ⇓	Date of onset (a)	End date (a) OR check here if continuing ⇓	Relationship to Drug (b) ⇓	Action Taken (c)	Sev-erity (d)	Out-come (e)	Treat-ment (f)

Use the following question to list additional symptoms from Questions 3 through 17.

18. Other

HHQUESTA

a. Number of the question above (Questions 3 – 17) to which this symptom applies: ☐☐

Specify symptom: ☐☐☐☐☐☐☐☐☐☐ HHSYMPTA ☐☐☐☐☐☐☐☐☐☐

☐☐/☐☐/HHBSYMA2 ☐	☐☐/☐☐/HHBSYMA3 ☐	4	5	6	7	8	9

b. Number of the question above (Questions 3 – 17) to which this symptom applies: ☐☐ HHQUESTB

Specify symptom: ☐☐☐☐☐☐☐☐☐☐ HHSYMPTB ☐☐☐☐☐☐☐☐☐☐

☐☐/☐☐/HHBSYMB2 ☐	☐☐/☐☐/HHBSYMB3 ☐	4	5	6	7	8	9

C. Hypoglycemia

		Yes	No
19. ***(Not applicable to SCR – Visit 1)*** Since the last clinic visit, has the participant experienced episodes of hypoglycemia?	HHEPISOD	☐	☐
If YES,			
a. Was this repeated mild hypoglycemia? (blood glucose <70 more than twice/week or 5 times/month)	HHREPEAT	☐	☐
b. Did the participant require help from someone else to bring blood sugar back to normal? (3rd party assistance due to loss of consciousness, confusion or severe lethargy)	HHRQHELP	☐	☐
➔ *If YES, complete form **SH, Severe Hypoglycemia***			
c. How many episodes of hypoglycemia (mild or severe) have occurred since the last clinic visit?	HHEPINUM ☐☐ episode(s)		

Reference Marks and Codes:

(a) Dates: Enter date in mm/dd/yyyy format. Enter 06 for month if unknown. Enter 15 for day if unknown. Do not enter date of diagnosis or onset for conditions or symptoms previously reported.

(b) Relationship to Drug: To be completed for baseline and follow-up visits only.
1-Definite
2-Probable
3-Possible
4-Unlikely
5-Unrelated

(c) Action taken: To be completed for baseline and follow-up visits only.
1-None
2-Discontinued
3-Reduced
4-Interrupted

(d) Severity: To be completed for baseline and follow-up visits only.
1- Mild: awareness of symptom but easily tolerated
2- Moderate: discomfort enough to cause interference with usual activity
3- Severe: incapacitating with inability to work or do usual activity

(e) Outcome: To be completed for baseline and follow-up visits only.
1-Recovered
2-Resolved, but sequelae / residual effect(s) remain
3-Still present
4-Death

(f)Treatment: To be completed for baseline and follow-up visits only.
1-None
2-Medication required; no hospitalization
3-Hospitalization required or prolonged; no medication required
4-Medication required; hospitalization required or prolonged
5-Other

TINSAL-T2D Stage 2 Form INELIG
Ineligibility at Baseline Form PATIENT

CLINIC
Clinic

Participant ID

1. Nickname	IENICKNA	
2. Visit date (mm/dd/yyyy)	IEVISITD	/ /
3. Staff ID	IESTAFFI	

Instructions: This form is to be completed during the baseline visit (Visit 3) in order to determine if some event has occurred between the screening and baseline visits that makes the participant ineligible to participate in the study. Checking any box indicates that the participant is ineligible.

A. Medical/Historical Eligibility Criteria

	Yes	
4. Participant has taken rosiglitazone (Avandia), pioglitazone (Actos), or extendin-4 (Byetta) in the last 6 months.	1	IEOTHRX
5. Pregnancy or lactation.	1	IEPREGNA
6. Participant requires oral corticosteroids within 3 months or recurrent continuous oral corticosteroid treatment (more than 2 weeks). *Note: inhaled or topical corticosteroids are acceptable in moderation at the discretion of the site investigator, with exclusion for excessive use, including suspected adrenal suppression or cushinoid appearance.*	1	IESTER
7. Use of weight loss drugs (e.g., Xenical (orlistat), Meridia (sibutramine), Acutrim (phenylpropanol-amine), or similar over the counter medications) within 3 months of screening.	1	IEWTRX
8. Surgery within 30 days of baseline visit.	1	IESURG
9. History of acquired immune deficiency syndrome or human immunodeficiency virus (HIV).	1	IEHIV
10. History of malignancy, except participants who have been disease-free for greater than 10 years, or whose only malignancy has been basal or squamous cell skin carcinoma.	1	IEHMALIG
11. History of unstable angina, myocardial infarction, cerebrovascular accident, transient ischemic attack or any revascularization – any of these within 6 months.	1	IECV
12. Chronic or continuous use (daily for more than 7 days) of nonsteroidal anti-inflammatory drugs within the past 2 months.	1	IENSAID
13. Use of warfarin (Coumadin), clopidogrel (Plavix), dipyridamole (Persantine), heparin or other anticoagulants.	1	IEANTICO
14. Use of probenecid (Benemid, Probalan), sulfinpyrazone (Anturane) or other uricosuric agents.	1	IEPROBEN
15. Diabetes medication has been adjusted within the past 8 weeks.	1	IEDIABET
16. History of tinnitus.	1	IETINNIT

TINSAL-T2D Stage 2 Form INTERIM
Interim visit

INVISIDT

Clinic (CLINIC) | Participant ID (PATIENT) | Visit date (mm/dd/yyyy)

1. Nickname INNICKNA
2. Staff ID INSTAFF
3. Visit location INVISLOC ☐1 Phone ☐2 In clinic ☐3 Other medical facility
4. Does visit require physical examination? ☐1 Yes ☐2 No
   If yes, fill out form PE INREQPE

Instructions: Complete at all non-scheduled visits after initial consent.

A. Reason for Visit

5. Reason for visit — **Check all that apply**

a. ☐1 Central laboratory test (blood or urine) INREASA
b. ☐1 Follow-up to local laboratory test (i.e., performed by PCP) INREASB
c. ☐1 Adverse event (or suspected AE) INREASC
d. ☐1 Medication dispensing INREASD
e. ☐1 Medical supplies (strips, monitors) INREASE
f. ☐1 Safety Visit (reason INREASGR _____) INREASG
g. ☐1 Other (specify INREASFS _____) INREASF

B. Vital Signs

6. Sitting blood pressure — Systolic / Diastolic

Record BP reading 3 only if first 2 readings vary by more than 10%.

a. BP reading 1 (after sitting 5 minutes) INBPS1 ___ / ___ INBPD1 mmHg
b. BP reading 2 (after waiting 1 minute) INBPS2 ___ / ___ INBPD2 mmHg
c. BP reading 3 (after waiting 1 minute) INBPS3 ___ / ___ INBPD3 mmHg

7. Heart rate INHEARTR ___ bpm

☐☐ **Clinic** ☐☐☐☐☐ **Participant ID** ☐☐/☐☐/☐☐☐☐ **Visit date (mm/dd/yyyy)**

C. Diabetes Medication and Rescue Therapy

8. Is there a change in diabetes therapy other than salsalate? ☐1 Yes ☐2 No

INCHANGE

If YES,

a. Reason for change:

INCHGRE

☐1 Adjusted based on home monitoring or by PCP
☐2 Met protocol criteria for rescue therapy
☐3 Hyperglycemia
☐4 Hypoglycemia
☐5 Other (specify INCHGRES _____)

b. Date of change in therapy: ☐☐/☐☐/☐☐☐☐ INCHGDT

c. What medication is the participant currently taking?

Metformin ☐1 Yes ☐2 No INMETF

Dose: ☐☐☐☐ mg INMETFD

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h INMETFF

☐7 Other (specify): ☐☐☐☐☐ INMETFFS

Insulin secretagogue ☐1 Yes ☐2 No ININSE

Dose: ☐☐☐☐ mg ININSED

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h ININSEF

☐7 Other (specify): ☐☐☐☐☐ ININSEFS

Insulin ☐1 Yes ☐2 No ININSU

Type: ☐1 Glargine ☐2 NPH/Lente ☐3 Regular ☐4 Humalog /Novalog ☐5 Ultralente ☐6 Other ININSUT

Dose: ☐☐☐ total units per day ININSUD

Clinic ☐☐ Participant ID ☐☐☐☐☐ Visit date (mm/dd/yyyy) ☐☐/☐☐/☐☐☐☐

C. Diabetes Medication and Rescue Therapy (continued)

Other ☐1 Yes ☐2 No INOTHE

Specify: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ INOTHES

Dose: ☐☐☐☐ mg INOTHED

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h INOTHEF

☐7 Other (specify): ☐☐☐☐☐ INOTHEFS

TINSAL-T2D Stage 2 Form MEDLOG
Study Medication Log

MEPAGENO

Clinic: CLINIC | Participant ID: PATIENT | Page No. ⇐

If this is the first time a log entry has been made for this participant, enter 01. If this page is an addition to a log that already exists, enter the next sequential page number.

Nickname MENICKNA

	Date (mm/dd/yyyy)	Staff ID	Action	Adjust /Stop Reason	Stop Perma-nently?	Total Daily Dose
1.	/ / MEDATE1	MESTAFF1	Start / Adjust / Stop MEACTI1	MEADJU1	1 Yes / 1 No MESTOP1	number of tablets METOTAL1
2.	/ / MEDATE2	MESTAFF2	Start / Adjust MEACTI2	MEADJU2	1 Yes / 1 No MESTOP2	number of tablets METOTAL2
3.	/ / MEDATE3	MESTAFF3	Start / Adjust MEACTI3	MEADJU3	1 Yes / 1 No MESTOP3	number of tablets METOTAL3
4.	/ / MEDATE4	MESTAFF4	Start / Adjust MEACTI4	MEADJU4	1 Yes / 1 No MESTOP4	number of t METOTAL4
5.	/ / MEDATE5	MESTAFF5	Start / Adjust MEACTI5	MEADJU5	1 Yes / 1 No MESTOP5	number of tablets METOTAL5

Reasons for adjustment:
01 – tinnitus
02 – headache
03 – GI side effects
04 – other side effects

Reasons for discontinuation:
05 – evidence of allergy to medication
06 – acute change in renal function
07 – intolerable adverse event
08 – pregnancy
09 – intercurrent illness (may be transient if condition resolves)
10 – new diagnosis of exclusionary medical condition
11 - other

TINSAL-T2D Stage 2 Form MH
Mild Hypoglycemia

Clinic CLINIC | Participant ID PATIENT | Date of form completion (mm/dd/yyyy) MHCOMPDT / | Hypoglycemic event number MHNUMBER

If only one MH form is completed for this participant on this date, enter 1.
For multiple forms completed for this participant on this date, use additional MH forms and label 1, 2, 3, etc.

Instructions: Complete this form each time a participant experiences a mild or moderate hypoglycemia episode.

1. Nickname MHNICKNA
2. Staff ID MHSTAFFI
3. Date of occurrence or recognition of hypoglycemic event (mm/dd/yyyy) MHOCCUDT / /
   a. If date uncertain, check here ⇒ MHUNCERT ☐1
4. Date reported to clinic (mm/dd/yyyy) MHREPODT / /

A. Clinical Manifestation

5. The hypoglycemia was
   a. associated with symptoms. MHSYMPTO ☐1
   b. detected by routine blood glucose monitoring. MHMONITO ☐1

If ASSOCIATED WITH SYMPTOMS,

Check all that apply:

i. Hunger MHHUNGER ☐1
ii. Anxiousness MHANXIOU ☐1
iii. Sweating MHSWEAT ☐1
iv. Shakiness MHSHAKIN ☐1
v. Heart pounding MHHEARTP ☐1
vi. Dizziness MHDIZZIN ☐1
vii. Trouble concentrating MHTROCON ☐1
viii. Trouble remembering words MHTROREM ☐1
ix. Other: MHOTHER ☐1

1. Specify: MHOSPE

Note that symptom "Blackout" removed from form; Variable=MHBLACKO

TINSAL-T2D Stage 2 Form MH
Mild Hypoglycemia

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Hypoglycemic event number
☐☐	☐☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐

A. Clinical Manifestation (Continued)

x. Were the low sugar symptoms that the participant had while participating in the TINSAL-T2D study similar to previous symptoms? ☐1 Yes ☐2 No **MHSIMIL**

If NO,

1. Describe how the hypoglycemia episode during the study was different from the participant's past experience(s): **MHDIFFDE**

_____

_____

_____

_____

_____

B. Blood Glucose Determination

6. Was the blood sugar documented near the time of the hypoglycemia? ☐1 Yes ☐2 No **MHBMEAS**

If YES,

a. What was the glucose value? ☐☐☐ **MHGLVALU** mg/dl

If documented more than once, enter the lowest value.

MHGLTIME
- ☐1 before treating
- ☐2 after treating
- ☐3 unknown

C. Potential Contributing Factors

7. Note any extenuating circumstances:

a. Missed meal **MHMISSME** ☐1

b. Greater than usual exercise **MHEXERC** ☐1

c. Increased dose of medications **MHINMEDS** ☐1

i. Specify which medications: **MHIMSPEC**

_____

_____

d. None **MHNONE** ☐1

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Hypoglycemic event number
☐☐	☐☐☐☐☐	☐☐/☐☐/☐☐☐☐	☐

C. Potential Contributing Factors (continued)

8. Has the participant previously had hypoglycemic events requiring the assistance of others? ☐1 Yes ☐2 No **MHASSIST**

If YES,

a. How many times has the participant needed the help of others? **MHASTIME** ☐☐ times

b. When was the most recent episode of low sugar requiring assistance? **MHASDATE** ☐☐/☐☐/☐☐☐☐

(mm/dd/yyyy – use 06 if the month is unknown; use 15 if the day is unknown.)

9. Has the participant had low sugar reactions that did not require the help of others? ☐1 Yes ☐2 No **MHLSREAC**

If YES,

a. Did the participant have symptoms in the past with low sugar reactions? ☐1 Yes ☐2 No **MHLSSYMP**

b. Did the participant have low sugar reactions detected by blood glucose monitoring without symptoms? ☐1 Yes ☐2 No **MHLSMONI**

c. About how often has the participant had low sugar reactions in the past 6 months? **MHLSOFTE** ☐☐ times

MHLSOFTS ☐1 per week ☐2 per month

10. Did you contact the primary care physician? ☐1 Yes ☐2 No **MHPCP**

a. What was the result? **MHPCPRES**

_____

_____

_____

_____

_____

TINSAL-T2D Stage 2 Form MH v.2
Mild Hypoglycemia

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Hypoglycemic event number
CLINIC	PATIENT	MHCOMPDT	MHNUMBER

If only one MH form is completed for this participant on this date, enter 1. For multiple forms completed for this participant on this date, use additional MH forms and label 1, 2, 3, etc. For each new date, start at 1.

Instructions: Complete this form each time a participant experiences a mild or moderate hypoglycemia episode.

1. Nickname MHNICKNA
2. Staff ID MHSTAFFI
3. Date of occurrence or recognition of hypoglycemic event (mm/dd/yyyy) MHOCCUDT
   a. If date uncertain, check here ⇒ MHUNCERT ☐1
4. Date reported to clinic (mm/dd/yyyy) MHREPODT

A. Clinical Manifestation

5. The hypoglycemia was
   a. associated with symptoms. MHSYMPTO ☐1
   b. detected by routine blood glucose monitoring. CLINIC ☐1

If ASSOCIATED WITH SYMPTOMS,

Check all that apply:

i. Hunger MHHUNGER ☐1
ii. Anxiousness MHANXIOU ☐1
iii. Sweating MHSWEAT ☐1
iv. Shakiness MHSHAKIN ☐1
v. Heart pounding MHHEARTP ☐1
vi. Dizziness MHDIZZIN ☐1
vii. Trouble concentrating MHTROCON ☐1
viii. Trouble remembering words MHTROREM ☐1
ix. Other: MHOTHER ☐1

1. Specify: MHOSPE

TINSAL-T2D Stage 2 Form MH v.2
Mild Hypoglycemia

☐☐ Clinic ☐☐☐☐☐ Participant ID ☐☐/☐☐/☐☐☐☐ Date of form completion (mm/dd/yyyy) ☐ Hypoglycemic event number

A. Clinical Manifestation (Continued)

x. Were the low sugar symptoms that the participant had while participating in the TINSAL-T2D study similar to previous symptoms? ☐1 Yes ☐2 No MHSIMIL

If NO,

1. Describe how the hypoglycemia episode during the study was different from the participant's past experience(s):

MHDIFFDE _____

_____

_____

_____

B. Blood Glucose Determination

6. Was the blood sugar documented near the time of the hypoglycemia? ☐1 Yes ☐2 No MHBMEAS

If YES,

a. What was the glucose value?

If documented more than once, enter the lowest value. MHGLVALU ☐☐☐ mg/dl

MHGLTIME
☐1 before treating
☐2 after treating
☐3 unknown

C. Potential Contributing Factors

7. Note any extenuating circumstances:

a. Missed meal MHMISSME ☐1

b. Greater than usual exercise MHEXERC ☐1

c. Increased dose of medications MHINMEDS ☐1

i. Specify which medications:

MHIMSPEC _____

_____

d. None MHNONE ☐1

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Hypoglycemic event number
☐☐	☐☐☐☐☐	☐☐/☐☐/☐☐☐☐	☐

C. Potential Contributing Factors (continued)

8. Has the participant previously had hypoglycemic events requiring the assistance of others? ☐1 Yes ☐2 No MHASSIST

If YES,

a. How many times has the participant needed the help of others? MHASTIME ☐☐ times

b. When was the most recent episode of low sugar requiring assistance? MHASDATE ☐☐/☐☐☐☐

(mm/dd/yyyy – use 06 if the month is unknown; use 15 if the day is unknown.)

9. Has the participant had low sugar reactions that did not require the help of others? ☐1 Yes MHLSREAC ☐2 No

If YES,

a. Did the participant have symptoms in the past with low sugar reactions? ☐1 Yes MHLSSYMP ☐2 No

b. Did the participant have low sugar reactions detected by blood glucose monitoring without symptoms? ☐1 Yes MHLSMONI ☐2 No

c. About how often has the participant had low sugar reactions in the past 6 months? MHLSOFTE ☐☐ times

MHLSOFTS ☐1 per week
☐2 per month

D. Follow-up

10. Were diabetes medications adjusted? ☐1 Yes MHMEDAD ☐2 No

➔*If YES, please record the change on a **VISIT or INTERIM form***

11. Medical Summary: MHMEDSUM _____

_____

_____

_____

_____

_____

_____

12. Did you contact the primary care physician? MHPCP ☐1 Yes ☐2 No

TINSAL-T2D Stage 2 Form PD
Protocol Deviation

PDCOMPDT

PDNUMBER

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Protocol deviation number
CLINIC	PATIENT		

If only one PD form is completed for this participant on this date, enter 1.
For multiple forms completed for this participant on this date, use additional PD forms and label 1, 2, 3, etc.

1. Nickname PDNICKNA
2. Staff ID PDSTAFFI

Instructions: Complete this form for each protocol deviation.

Protocol deviation

3. Date of protocol deviation (mm/dd/yyyy) PDDEVIDT

4. Nature of deviation (check at least one):

   a. An ineligible participant was randomized without permission from the medical monitor. ☐1 PDRNDWOP

   b. An ineligible participant was randomized with permission from the medical monitor. ☐1 PDRNDWIP

   c. An incorrect dosage was given to the participant. ☐1 PDINCORR

   d. The participant's treatment assignment became unmasked to the clinician(s). ☐1 PDUNMASC

   e. The participant's treatment assignment became unmasked to the participant. ☐1 PDUNMASP

   f. Late visit ☐1 PDLATEVI

   g. Other (e.g., lab tests not performed, informed consent not signed) ☐1 PDOTHER

5. Details of protocol deviation (include assessment of participant harm, if any):

PDDETAIL

PDDETAI2

TINSAL-T2D Stage 2 Form PE
Physical Examination

PEVISITD

Clinic (CLINIC) | Participant ID (PATIENT) | Visit date (mm/dd/yyyy)

1. Nickname MSTAFFID — PENICKNA
2. Visit ID — PEVISITI
   RUN=Visit 2
   W14=Visit 7
   W26=Visit 9
   INT=Interim
3. Staff ID MSTAFFID — PESTAFFI

Instructions: Complete physical exam form at run-in, at interim visits (optional) and at the final study visit (Week 14 of Stage 1 or Week 26 of Stage 2).

A. General Physical Exam

		Normal	Abnormal, not clinically significant	Abnormal, clinically significant
4. HEENT	PEHEENT	☐	☐	☐
5. Thyroid	PETHYROI	☐	☐	☐
6. Lungs	PELUNGS	☐	☐	☐

a. Auscultation of lungs PEAUSCUL

☐ Normal ☐ Basilar rales only ☐ Rales greater than basilar ☐ Wheezing

		Normal	Abnormal, not clinically significant	Abnormal, clinically significant
7. Heart	PEHEART	☐	☐	☐

a. ***If ABNORMAL, CLINICALLY SIGNIFICANT, specify*** PEHEARTS _____

		Normal	Abnormal, not clinically significant	Abnormal, clinically significant
8. Abdomen	PEABDOME	☐	☐	☐

a. ***If ABNORMAL,*** hepatomegaly present ☐ Yes ☐ No PEHEPATO

If this is not a run-in visit, skip to Question 9.

b. Stool guaiac PESTOOLG ☐ Digital Rectal Exam ☐ Hemoccult card

c. Stool guaiac results PESTOOLR ☐ Normal ☐ Abnormal

If stool guaiac ABNORMAL,

d. Specify cause PESTOOLS _____

TINSAL-T2D Stage 2 Form PE
Physical Examination

Clinic ☐☐ Participant ID ☐☐☐☐☐ Visit date (mm/dd/yyyy) ☐☐/☐☐/☐☐☐☐

A. General Physical Exam (continued)

		Normal	Abnormal, not clinically significant	Abnormal, clinically significant
9. Skin	PESKIN	☐	☐	☐

If skin ABNORMAL,

a. Acanthosis nigricans ☐ Yes ☐ No PEACANTH

b. Rash MRASH ☐ Yes ☐ No PERASH

If YES,

i. Possibly drug related? MRASHRX ☐ Yes ☐ No PEPOSSIB

ii. Infectious? ☐ Yes ☐ No PEINFECT

Excluded if i or ii present at run-in visit

B. Edema Exam

	Left Foot (mark one only)	Right Foot (mark one only)
10. Grade pre-tibial edema based on today's visit	☐ None ☐ Trace ☐ 2+ PEEDEMA1	☐ None ☐ Trace ☐ 2+ PEEDEMA2

C. Foot Exam

		Left Foot			Right Foot			
11. Ulceration	PEULCERL	☐ Present	☐ Absent		☐ Present	☐ Absent		PEULCERR
12. Ankle reflexes	PEANKLEL	☐ Present	☐ Present/ Reinforcement	☐ Absent	☐ Present	☐ Present/ Reinforcement	☐ Absent	PEANKLER
13. 10gm filament	PE10GMFL	☐ Present (≥ 8)	☐ Reduced (1–7)	☐ Absent (0)	☐ Present (≥ 8)	☐ Reduced (1–7)	☐ Absent (0)	PE10GMFR

TINSAL-T2D Stage 2 Form PE v2
Physical Examination

PEVISITD

Clinic: CLINIC ☐☐ | Participant ID: PATIENT ☐☐☐☐☐ | Visit date (mm/dd/yyyy): ☐☐/☐☐/☐☐☐☐

1. Nickname	PENICKNA	☐☐☐☐☐☐	
2. Visit ID	PEVISITI	☐☐☐	RUN=Visit 2 W48=Visit 11 INT=Interim
3. Staff ID	PESTAFFI	☐☐☐	

Instructions: Complete physical exam form at run-in, at interim visits (optional) and at the final study visit (Week 48).

A. General Physical Exam

		Normal	Abnormal, not clinically significant	Abnormal, clinically significant
4. HEENT	PEHEENT	☐	☐	☐
5. Thyroid	PETHYROI	☐	☐	☐
6. Lungs	PELUNGS	☐	☐	☐

a. Auscultation of lungs PEAUSCUL

☐ Normal ☐ Basilar rales only ☐ Rales greater than basilar ☐ Wheezing

		Normal	Abnormal, not clinically significant	Abnormal, clinically significant
7. Heart	PEHEART	☐	☐	☐

a. ***If ABNORMAL, CLINICALLY SIGNIFICANT, specify*** PEHEARTS _____

8. Was EKG performed? PEEKG ☐ Yes ☐ No

a. ***If NO, why not?*** PEEKGWHY _____

TINSAL-T2D Stage 2 Form PE v2
Physical Examination

Clinic ☐☐ Participant ID ☐☐☐☐☐ Visit date (mm/dd/yyyy) ☐☐/☐☐/☐☐☐☐

A. General Physical Exam (continued)

		Normal	Abnormal, not clinically significant	Abnormal, clinically significant
9. Abdomen	PEABDOME	☐	☐	☐

a. ***If ABNORMAL,*** hepatomegaly present ☐ Yes ☐ No PEHEPATO

If this is not a run-in visit, skip to Question 9.

b. Stool guaiac PESTOOLG ☐ Digital Rectal Exam ☐ Hemoccult card

c. Stool guaiac results PESTOOLR ☐ Normal ☐ Abnormal

If stool guaiac ABNORMAL,

d. Specify cause PESTOOLS _____

10. Skin	PESKIN	☐	☐	☐

If skin ABNORMAL,

a. Acanthosis nigricans PEACANTH ☐ Yes ☐ No

b. Rash PERASH ☐ Yes ☐ No

If YES,

i. Possibly drug related? ☐ Yes ☐ No PEPOSSIB

ii. Infectious? ☐ Yes ☐ No PEINFECT

Excluded if i or ii present at run-in visit

B. Edema Exam

	Left Foot *(mark one only)*	Right Foot *(mark one only)*
11. Grade pre-tibial edema based on today's visit	☐ None ☐ Trace ☐ 2+ PEEDEMA1	☐ None ☐ Trace ☐ 2+ PEEDEMA2

Clinic ☐☐ Participant ID ☐☐☐☐☐ Visit date (mm/dd/yyyy) ☐☐/☐☐/☐☐☐☐

C. Foot Exam

	Left Foot			Right Foot		
12. Ulceration	PEULCERL ☐ Present	☐ Absent		☐ Present	☐ Absent	PEULCERR
13. Ankle reflexes	PEANKLEL ☐ Present	☐ Present/ Reinforcement	☐ Absent	☐ Present	☐ Present/ Reinforcement	☐ Absent PEANKLER
14. 10gm filament	PE10GMFL ☐ Present (≥ 8)	☐ Reduced (1–7)	☐ Absent (0)	☐ Present (≥ 8)	☐ Reduced (1–7)	☐ Absent (0) PE10GMFR

TINSAL-T2D Stage 2 Form SAE
Serious Adverse Event

SACOMPDT

SANUMBER

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	SAE number
CLINIC	PATIENT		

If only one SAE form is completed for this participant on this date, enter 1.
For multiple forms completed for this participant on this date, use additional SAE forms and label 1, 2, 3, etc.

1. Nickname SANICKNA
2. Staff ID SASTAFFI

Instructions: Complete this form within 24 hours of each serious adverse event.

Serious Adverse Event Information

3. Event – short description SASDESCR
4. Date reported to clinic (mm/dd/yyyy) SAREPODT
5. Date of onset (mm/dd/yyyy) SAONSEDT
6. Date of resolution (mm/dd/yyyy) SARESODT

or continuing 1 SACONTIN

7. Was SAE anticipated? 1 Yes 2 No SAANTICI
8. Type of adverse event *(check all that apply)*

- 1 Death SATDEATH
- 1 A life-threatening event SATLIFET
- 1 Inpatient hospitalization or prolongation of existing hospitalization SATINPAT
- 1 A persistent or significant disability/incapacity SATPERSI
- 1 A congenital anomaly or birth defect SATCONGE
- 1 Important medical event based upon appropriate medical judgement SATIMPOR

TINSAL-T2D Stage 2 Form SAE
Serious Adverse Event

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	SAE number
		/ /	

Serious Adverse Event Information (continued)

9. Outcome *(check all that apply)*

SAODEC ☐ 1 Deceased

If Deceased,

SAODECDT a. Date of death ☐☐/☐☐/☐☐☐☐

SAODECLO b. Location of death

SAOHOSPI ☐ 1 Required or prolonged hospitalization

SAODISAB ☐ 1 Resulted in permanent or severe disability

SAOINTER ☐ 1 Required intervention to prevent permanent damage or disability

10. Relationship to study intervention *(check one)*

☐ 1 Not related

SARELATI ☐ 2 Unlikely

☐ 3 Suspected (reasonable possibility)

☐ 4 Probable

11. Body system affected *(check all that apply)*

SABCIRCU ☐ 1 Circulatory system

☐ 1 Respiratory system SABRESPI

SABNERVO ☐ 1 Nervous system

☐ 1 Musculoskeletal system SABMUSCU

SABSKIN ☐ 1 Skin or subcutaneous tissue

☐ 1 Digestive system SABDIGES

SABGENIT ☐ 1 Genitourinary system

☐ 1 Unknown SABUNKNO

SABOTHE ☐ 1 Other (specify) → SABOTHES

TINSAL-T2D Stage 2 Form SAE
Serious Adverse Event

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	SAE number
☐☐	☐☐☐☐☐	☐☐/☐☐/☐☐☐☐	☐

Serious Adverse Event Information (continued)

12. Action taken/corrective therapy *(check all that apply)*

SAANONE ☐ 1 None

SAASELFT ☐ 1 Self treatment or OTC therapy

SAAOFFIC ☐ 1 Office, clinic, ER, or outpatient visit

SAAINPAT ☐ 1 Inpatient visit, hospital admission

SAAPRESC ☐ 1 Prescription medication

SAAPROCE ☐ 1 Procedure performed

SAAOTHE ☐ 1 Other *(specify)* → SAAOTHES

13. Action taken regarding coded study medication

SASTUDYM

☐ 1 N/A, previously discontinued
☐ 2 No action taken
☐ 3 Dose reduced
☐ 4 Dose increased
☐ 5 Interrupted
☐ 6 Drug stopped

*If coded study medication stopped for ≥ 72 hours, complete Form **MEDLOG, Coded Study Medication Log***

14. Recovery *(check one)* SARECOVE

☐ 1 Recovered / resolved
☐ 2 Recovering / resolving with no sequelae
☐ 3 Not recovered / not resolved
☐ 4 Recovering / resolving with sequelae
☐ 5 Fatal
☐ 6 Unknown

15. Description of event

SALDESCR _____

SALDESC2 _____

_____

_____

_____

TINSAL-T2D Stage 2 Form SAE
Serious Adverse Event

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	SAE number
		/ /	

Serious Adverse Event Information (continued)

16. Relevant history *(including preexisting medical conditions)*

SAHISTOR

SAHISTO2

17. List concomitant medications (excluding study medication) taken at the time the event occurred.

	Medication	Dose	Frequency
a.	SAMEDICA	SADOSEA	SAFREQA
b.	SAMEDICB	SADOSEB	SAFREQB
c.	SAMEDICC	SADOSEC	SAFREQC
d.	SAMEDICD	SADOSED	SAFREQD

TINSAL-T2D Stage 2 Form SAFETY
Safety Alert Follow-up

SYTRACKN

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Tracking number
CLINIC	PATIENT	SYCOMPDT	

Instructions: Complete this form each time you receive a safety e-mail that requires a letter be sent to the participant's PCP.

1. Nickname SYNICKNA
2. Staff ID SYSTAFF
3. Date e-mail received SYEMAILD __/__/____

4. Reason for Alert SYREASON
   - ☐ 1 Blood Pressure
   - ☐ 2 LDL
   - ☐ 3 Microalbumin/creatinine ratio
   - ☐ 4 Plasma Fasting Glucose
   - ☐ 5 HbA1c
   - ☐ 6 Triglycerides

Letter to PCP

5. Letter sent to PCP ☐ 1 Yes ☐ 2 No SYLETTER

IF YES,

a. Seen by PCP ☐ 1 Yes ☐ 2 No ☐ 3 Unknown SYSEEPCP

IF YES,

i. Date __/__/____ SYPCPDT

ii. Outcome SYPCPOUT
- ☐ 1 Watchful waiting
- ☐ 2 Non-Study medications adjusted ⇒ **update CONMED form**
- ☐ 3 Withdrawn from study ⇒ **fill out STATUS form**
- ☐ 4 Other

Specify: SYPCPOUS _____

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Tracking number
☐☐	☐☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐☐☐

PI Evaluation

6. PI evaluation of participant's safety SYPINARR

_____

_____

_____

_____

TINSAL-T2D Stage 2 Form SAFETY v2
Safety Alert Follow-up

SYTRACKN

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Tracking Id
CLINIC	PATIENT	SYCOMPDT	

Instructions: Complete this form within 7 days of receiving a safety alert e-mail.

1. Nickname SYNICKNA
2. Staff ID SYSTAFF
3. Date e-mail received SYEMAILD

4. Reason for alert SYREASON

- ☐ 1 Blood Pressure
- ☐ 2 LDL
- ☐ 3 Microalbumin/creatinine ratio
- ☐ 4 Plasma Fasting Glucose
- ☐ 5 HbA1c
- ☐ 6 Triglycerides
- ☐ 7 eGFR
- ☐ 8 Developed Exclusionary Condition

Specify: SYREAOS

5. Visit that triggered alert SYVISIT

PI Evaluation

6. Outcome SYPCPOUT

- ☐ 1 Watchful waiting
- ☐ 2 Non-Study medications adjusted ⇒ **update CONMED form**
- ☐ 5 Study medication adjusted ⇒ **fill out MEDLOG form**
- ☐ 3 Withdrawn from study medication ⇒ **fill out MEDLOG form**
- ☐ 4 Other

Specify: SYPCPOUS

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Tracking Id
☐☐	☐☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐☐☐

PI Evaluation (continued)

7. PI narrative SYPINARR

Letter to PCP (to be completed at next visit)

8. Letter sent to PCP ☐ 1 Yes ☐ 2 No SYLETTER

IF YES,

a. Seen by PCP ☐ 1 Yes ☐ 2 No ☐ 3 Unknown SYSEEPCP

IF YES,

i. Date ☐☐ / ☐☐ / ☐☐☐☐ SYPCPDT

TINSAL-T2D Stage 2 Form SCREEN
Screening and Patient History Form

Clinic
CLINIC

Participant ID
PATIENT

1. Nickname	SCNICKNA	
2. Visit date (mm/dd/yyyy)	SCVISIDT	/ /
3. Staff ID	SCSTAFF	

Instructions: This form is to be completed to assess eligibility for the run-in after the participant has signed the consent for screening. Checking a shaded box indicates that the participant is ineligible. Complete all items on the form even if the participant is ineligible. However, if it is determined that the participant is ineligible before screening labs are drawn, do not collect screening labs or measure vital signs. Leave questions 36-39 blank.

A. Demographic Eligibility Criteria

4. Was informed consent signed and dated? SCCONSEN 1 Yes 2 No

➔ ***IF NO, STOP.***

5. Age eligibility

   a. Date of birth (mm/dd/yyyy) SCDOB / /

   b. Age: SCAGE years

   c. Age 18-74? SCAGE18 1 Yes 2 No

6. Gender SCGENDER 1 Male 2 Female

B. Diabetes Eligibility Criteria

7. Date of diabetes diagnosis (mm/dd/yyyy – mark day as 15 if unknown) / / SCDIAGDT

8. Does the participant have type 1 diabetes (by medical history)? 1 Yes 2 No SCTYPE1

9. Has the participant ever experienced ketoacidosis? 1 Yes 2 No SCKETOAC

10. Is the participant currently taking insulin, or has the participant used insulin for > 30 days within the past year? 1 Yes 2 No SCINSU30

Clinic ☐☐ Participant ID ☐☐☐☐☐

B. Diabetes Eligibility Criteria (continued)

11. What diabetes medication is the participant currently taking?

Metformin ☐1 Yes ☐2 No SCMETF

Dose: ☐☐☐☐ mg SCMETFD

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h SCMETFF

☐7 Other (specify): ☐☐☐☐☐ SCMETFFO

Insulin secretagogue ☐1 Yes ☐2 No SCINSS

Specify: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ SCINSSS

Dose: ☐☐☐☐ mg SCINSSD

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h SCINSSF

☐7 Other (specify): ☐☐☐☐☐ SCINNSFO

Alpha-glucosidase inhibitor ☐1 Yes ☐2 No SCAGIN

Type: ☐1 Acarbose ☐2 Miglitol SCAGINT

Dose: ☐☐☐☐ mg SCAGIND

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h SCAGINF

☐7 Other (specify): ☐☐☐☐☐ SCAGINFO

DPP-4 inhibitor (Januvia™) ☐1 Yes ☐2 No SCDPP

Dose: ☐☐☐☐ mg SCDPPD

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h SCDPPF

☐7 Other (specify): ☐☐☐☐☐ SCDPPFO

Clinic ☐☐ Participant ID ☐☐☐☐☐

B. Diabetes Eligibility Criteria (continued)

Other ☐1 Yes ☐2 No SCOTHE

Specify: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ SCOTHES

Dose: ☐☐☐☐ mg SCOTHED

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h SCOTHEF

☐7 Other (specify): ☐☐☐☐☐ SCOTHEFS

12. Has the participant taken rosiglitazone (Avandia), pioglitazone (Actos), or extendin-4 (Byetta) in the last 6 months? 1 Yes 2 No SCOTHRX

13. Is the participant on any diabetes therapy other than the following? 1 Yes 2 No SCDBTHER

- Diet and exercise therapy **OR**
- Monotherapy with metformin, an insulin secretagogue, or an alpha-glucosidase inhibitor **OR**
- Low-dose combination of these at ≤ 50% of maximal dose (see "Appendix: Recommended Dosing of Diabetic Medication" in the TINSAL-T2D Protocol) **OR**
- Combination of two of these at ≤ 100% of maximal dose for each **OR**
- Sitagliptin (Januvia™) and metformin

If NO,

a. Has dosing been stable for 8 weeks prior to screening? 1 Yes 2 No SCSTABLE

b. Is the participant on combination therapy consisting of two of the following: metformin, an insulin secretagogue, or an alpha-glucosidase inhibitor, **AND** one or both doses are > 50% of maximal dose? 1 Yes 1 No SCMAXDOS

TINSAL-T2D Stage 2 Form SCREEN
Screening and Patient History Form

Clinic | Participant ID

C. Medical/Historical Eligibility Criteria

Checking a shaded box indicates that the participant is ineligible.

	Yes	No	
14. The participant is male. ***OR*** The participant is female without child-bearing potential. ***OR*** The participant is female with child-bearing potential and has agreed to use an appropriate contraceptive method (hormonal, IUD, or diaphragm).	1	2	SCCONTRA
15. History of severe diabetic neuropathy including autonomic neuropathy, gastroporesis, or lower limb ulceration or amputation.	1	2	SCNEURO
16. Pregnancy or lactation.	1	2	SCPREGNA
17. Participant requires oral corticosteroids within 3 months or recurrent continuous oral corticosteroid treatment (more than 2 weeks).	1	2	SCSTER
Note: inhaled or topical corticosteroids are acceptable in moderation at the discretion of the site investigator, with exclusion for excessive use, including suspected adrenal suppression or cushinoid appearance.			
18. Use of weight loss drugs (e.g., Xenical (orlistat), Meridia (sibutramine), Acutrim (phenylpropanol-amine), or similar over the counter medications) within 3 months of screening.	1	2	SCWTRX
19. Intentional weight loss of ≥ 10 lbs in the previous 6 months.	1	2	SCWTLOSS
20. Surgery within 30 days of screening.	1	2	SCSURG
21. History of chronic liver disease including hepatitis B or C.	1	2	SCLIVER
22. History of peptic ulcer or endoscopy demonstrated gastritis.	1	2	SCULCER
23. History of acquired immune deficiency syndrome or human immunodeficiency virus (HIV).	1	2	SCHIV
24. History of malignancy, except participants who have been disease-free for greater than 10 years, or whose only malignancy has been basal or squamous cell skin carcinoma.	1	2	SCMALIG

Clinic ☐☐ Participant ID ☐☐☐☐☐

C. Medical/Historical Eligibility Criteria (continued)

	Yes	No	
25. New York Heart Association Class III or IV cardiac status or hospitalization for congestive heart failure.	1	2	SCCHD
26. History of unstable angina, myocardial infarction, cerebrovascular accident, transient ischemic attack or any revascularization – any of these within 6 months.	1	2	SCCV
27. Uncontrolled hypertension (defined as systolic BP >150 mmHg or diastolic BP >95 mmHg on three or more assessments on more than one day)	1	2	SCHIBP
Participant may be treated for hypertension and invited to re-screen once in control.			
28. History of drug or alcohol abuse, or current weekly alcohol consumption >10 units/week (1 unit = 1 beer, 1 glass of wine, 1 cocktail containing 1 oz alcohol).	1	2	SCDRUGS
29. Poor mental function or any other reason to expect participant difficulty in complying with the requirements of the study.	1	2	SCCOMPLY
30. Previous allergy to aspirin.	1	2	SCALLERG
31. Chronic or continuous use (daily for more than 7 days) of nonsteroidal anti-inflammatory drugs within the past 2 months.	1	2	SCNSAID
32. Use of warfarin (Coumadin), clopidogrel (Plavix), dipyridamole (Persantine), heparin or other anticoagulants	1	2	SCANTICO
33. Use of probenecid (Benemid, Probalan), sulfinpyrazone (Anturane) or other uricosuric agents.	1	2	SCPROBEN
34. Patient able to complete the study protocol in the opinion of the investigator.	1	2	SCCOMPLE
35. History of chronic tinnitus.	1	2	SCTINNIT

Clinic ☐☐ Participant ID ☐☐☐☐☐

D. Weight and Vital Signs

36. Sitting blood pressure Systolic / Diastolic

Record BP reading 3 only if first 2 readings vary by more than 10%.

a. BP reading 1 (after sitting 5 minutes) SCSBP1 ☐☐☐/☐☐☐ mmHg SCDBP1

b. BP reading 2 (after waiting 1 minute) SCSBP2 ☐☐☐/☐☐☐ mmHg SCDBP2

c. BP reading 3 (after waiting 1 minute) SCSBP3 ☐☐☐/☐☐☐ mmHg SCDBP3

Participants with uncontrolled hypertension (defined as systolic blood pressure >150 mmHg or diastolic blood pressure >95 mmHg on three or more assessments on more than one day) are not eligible.

37. Heart rate ☐☐☐ bpm SCHEARTR

If Dinamap® is used for both BP and heart rate, record first heart rate measurement.

38. Anthropometrics

For weight, record Measure 3 only if first 2 measurements are not within 0.2 kilograms.

a. Weight ☐☐☐.☐ kg SCWEIGH1 ☐☐☐.☐ kg SCWEIGH2 ☐☐☐.☐ kg SCWEIGH3

Clinic ☐☐ Participant ID ☐☐☐☐☐

E. If participant meets all above requirements, proceed with eligibility laboratory screening.

	Yes	No	
39. Participant meets laboratory eligibility criteria as follows.	☐ 1	☐ 2	SCLABEL

- Serum creatinine ≤1.4 for women and ≤1.5 for men AND eGFR ≥60
  - eGFR (ml/min/1.73m^2)=186 x (S_{cr})$^{-1.154}$ x (age)$^{-0.203}$ x (0.742 if female) x (1.210 if African American) (conventional units)
- Hemoglobin ≥12 (males) or ≥10 (females) g/dL
- Platelets ≥100,000 cu mm
- AST (SGOT) ≤ 2.50 x ULN and ALT (SGPT) ≤ 2.50 x ULN
- Total bilirubin ≤1.5 x ULN
- Triglycerides ≤500 mg/dL
- FPG ≤ 225 mg/dL
- HbA1c ≥ 7.5% and ≤ 9.5% (Participant is on combination therapy consisting of two of the following: metformin, an insulin secretagogue, or an alpha-glucosidase inhibitor, **AND** one or both doses are > 50% of maximal dose)
- HbA1c ≥ 7% and ≤ 9.5% (All other participants)
- Urine creatinine ≤300 mcg/mg Cr

a. Date verification received from laboratory (mm/dd/yyyy) ☐☐/☐☐/☐☐☐☐ SCLABDT

F. Eligibility for Run-in

	Yes	No	
40. Participant meets eligibility for run-in ***(All shaded boxes must be blank)***	☐ 1	☐ 2	SCELIG

G. Participant's Ethnicity

41. Is the participant Spanish/Hispanic/Latino? ☐ 1 Yes ☐ 2 No SCLATIN

Clinic ☐☐ Participant ID ☐☐☐☐☐

H. Participant's Race

42. What is the participant's race? ***Mark one or more races to indicate what this person considers himself/herself to be.***

a. ☐ 1 White SCWHITE

b. ☐ 1 Black or African American SCBLACK

c. ☐ 1 American Indian or Alaska Native SCAIAN

d. ☐ 1 Asian SCASIAN

e. ☐ 1 Hawaiian or Pacific Islander SCHIPI

f. ☐ 1 Some other race. SCORACE
Print race ⇒ SCORACES ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

I. Family History

43. Is there a history of any of the following conditions in the participant's biological father?

	Yes, before age 60	Yes, age 60 or older	Yes, age unknown	No	Unknown	
a. Coronary heart disease, heart attack, or stroke	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	SCFHXCVD
b. Type 1 diabetes	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	SCFHXT1D
c. Type 2 diabetes	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	SCFHXT2D

Clinic ☐☐ Participant ID ☐☐☐☐☐

I. Family History (continued)

44. Is there a history of any of the following conditions in the participant's biological mother?

	Yes, before age 60	Yes, age 60 or older	Yes, age unknown	No	Unknown	
a. Coronary heart disease, heart attack, or stroke	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	SCMHXCVD
b. Type 1 diabetes	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	SCMHXT1D
c. Type 2 diabetes	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	SCMHXT2D

45. Is there a history of any of the following conditions in the participant's biological siblings?

	Yes. Occurred in at least one sibling before age 60	Yes. Did not occur in any sibling before age 60	Yes, age(s) unknown	No	Unknown	
a. Coronary heart disease, heart attack, or stroke	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	SCSHXCVD
b. Type 1 diabetes	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	SCSHXT1D
c. Type 2 diabetes	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	SCSHXT2D

TINSAL-T2D Stage 2 Form SF-36 (English)
Health Status Survey

SFVISIT

Clinic CLINIC | **Participant ID** PATIENT | **Visit ID**

BAS=Visit 3
W14=Visit 7
W26=Visit 9

1. Nickname	SFNICKNA	
2. Visit date (mm/dd/yyyy) WVISDT	SFVISITD	/ /
3. Staff ID WSTAFFID	SFSTAFFI	

Instructions: The following pages are to be completed by the patient.

TINSAL-T2D Stage 2 Form SF-36 (English)
Health Status Survey

Clinic	Participant ID	Visit ID	BAS=Visit 3 W14=Visit 7 W26=Visit 9
☐☐	☐☐☐☐☐	☐☐☐	

Your Health and Well-Being

Instructions: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Thank you for completing this survey!

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

1. In general, would you say your health is: SFHEALTH

- ☐ 1 Excellent
- ☐ 2 Very Good
- ☐ 3 Good
- ☐ 4 Fair
- ☐ 5 Poor

2. Compared to one year ago, how would you rate your health in general now? SFLASTYR

- ☐ 1 Much better now than one year ago
- ☐ 2 Somewhat better now than one year ago
- ☐ 3 About the same as one year ago
- ☐ 4 Somewhat worse now than one year ago
- ☐ 5 Much worse now than one year ago

TINSAL-T2D Stage 2 Form SF-36 (English)
Health Status Survey

Clinic	Participant ID	Visit ID
☐☐	☐☐☐☐☐	☐☐☐

BAS=Visit 3
W14=Visit 7
W26=Visit 9

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Activities:	Yes, limited a lot	Yes, limited a little	No, not limited at all	
a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	1	2	3	SFVIGORO
b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3	SFMODERA
c. Lifting or carrying groceries	1	2	3	SFLIFTIN
d. Climbing several flights of stairs	1	2	3	SFCLIMBS
e. Climbing one flight of stairs	1	2	3	SFCLIMB1
f. Bending, kneeling, or stooping	1	2	3	SFBENDIN
g. Walking more than a mile	1	2	3	SFWALK1M
h. Walking several hundred yards	1	2	3	SFWALKSB
i. Walking one hundred yards	1	2	3	SFWALK1B
j. Bathing or dressing yourself	1	2	3	SFBATHIN

TINSAL-T2D Stage 2 Form SF-36 (English)
Health Status Survey

Clinic	Participant ID	Visit ID

BAS=Visit 3
W14=Visit 7
W26=Visit 9

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time	
a. Cut down the amount of time you spent on work or other activities	1	2	3	4	5	SF4CUTDO
b. Accomplished less than you would like	1	2	3	4	5	SF4ACCOM
c. Were limited in the kind of work or other activities	1	2	3	4	5	SF4LIMIT
d. Had difficulty performing the work or other activities (for example, it took extra effort)	1	2	3	4	5	SF4DIFFI

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time	
a. Cut down the amount of time you spent on work or other activities	1	2	3	4	5	SF5CUTDO
b. Accomplished less than you would like	1	2	3	4	5	SF5ACCOM
c. Did work or other activities less carefully than usual	1	2	3	4	5	SF5LESSC

6. During the past 4 weeks , to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

- [ ] 1 Not at all
- [ ] 2 Slightly
- [ ] 3 Moderately
- [ ] 4 Quite a bit
- [ ] 5 Extremely

SFSOCIEX

7. How much bodily pain have you had during the past 4 weeks?

- [ ] 1 None
- [ ] 2 Very mild
- [ ] 3 Mild
- [ ] 4 Moderate
- [ ] 5 Severe
- [ ] 6 Very severe

SFPAIN

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

1	Not at all	
2	A little bit	SFINTERF
3	Moderately	
4	Quite a bit	
5	Extremely	

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks -

	All of the time	Most of the time	Some of the time	A Little of the time	None of the time	
a. Did you feel full of life?	1	2	3	4	5	SFFULPEP
b. Have you been very nervous?	1	2	3	4	5	SFNERVOU
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	SFDUMPS
d. Have you felt calm and peaceful?	1	2	3	4	5	SFCALM
e. Did you have a lot of energy?	1	2	3	4	5	SFENERGY

	All of the time	Most of the time	Some of the time	A little of the time	None of the time	
f. Have you felt downhearted and depressed?	1	2	3	4	5	SFBLUE
g. Did you feel worn out?	1	2	3	4	5	SFWORN
h. Have you been a happy person?	1	2	3	4	5	SFHAPPY
i. Did you feel tired?	1	2	3	4	5	SFTIRED

10. During the <u>past 4 weeks</u>, how much of the time have your <u>physical health or emotional problems</u> interfered with your social activities (like visiting with friends, relatives, etc.)?

- 1 All of the time
- 2 Most of the time
- 3 Some of the time — SFSOCITM
- 4 A little of the time
- 5 None of the time

TINSAL-T2D Stage 2 Form SF-36 (English)
Health Status Survey

Clinic	Participant ID	Visit ID
☐☐	☐☐☐☐☐	☐☐☐

BAS=Visit 3
W14=Visit 7
W26=Visit 9

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False	
a. I seem to get sick a little easier than other people	1	2	3	4	5	SFSICK
b. I am as health as anybody I know	1	2	3	4	5	SFHELTHY
c. I expect my health to get worse	1	2	3	4	5	SFWORSE
d. My health is excellent	1	2	3	4	5	SFEXCELL

THANK YOU FOR COMPLETING THESE QUESTIONS!

TINSAL-T2D Stage 2 Form SH
Severe Hypoglycemia

SHCOMPDT

SHNUMBER

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Hypoglycemic event number
CLINIC	PATIENT		

If only one SH form is completed for this participant on this date, enter 1.
For multiple forms completed for this participant on this date, use additional SH forms and label 1, 2, 3, etc.

Instructions: Complete this form each time a participant experiences a severe hypoglycemia episode requiring assistance as specified in Chapter 8 of the Manual of Operations.

1. Nickname SHNICKNA
2. Staff ID SHSTAFFI
3. Date of occurrence or recognition of hypoglycemic event (mm/dd/yyyy) SHOCCUDT
   a. If date uncertain, check here ⇒ ☐1 SHUNCERT
4. Date reported to clinic (mm/dd/yyyy) SHREPODT

A. Clinical Manifestation

5. Check all symptoms or signs which occurred:

a.	SHSLOSSC	☐1	Loss of consciousness
b.	SHSSEIZU	☐1	Seizure
c.	SHSSUSPE	☐1	Suspected seizure
d.	SHSUNUSU	☐1	Unusual difficulty in awakening
e.	SHSIRRAT	☐1	Irrational
f.	SHSUNCON	☐1	Uncontrollable behavior
g.	SHSCONFU	☐1	Confusion
h.	SHSMEMOR	☐1	Memory loss
i.	SHSOTHE	☐1	Other, specify: SHSOTHES _____ _____ _____
j.	SHSNONE	☐1	None

TINSAL-T2D Stage 2 Form SH
Severe Hypoglycemia

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Hypoglycemic event number
☐☐	☐☐☐☐☐	☐☐/☐☐/☐☐☐☐	☐

B. Blood Glucose Determination

6. Was the blood glucose measured BEFORE treatment? SHBMEASD ☐1 Yes ☐2 No ☐3 Unknown

If YES,

a. By whom? SHBBYWHO
- ☐1 Participant
- ☐2 Medical care personnel
- ☐3 Other

b. Record measurement ☐☐☐ mg/dl SHBMEAST
OR, if UNKNOWN, check here ⇒ ☐1 SHBUNKNO

c. Method used SHBMETHO
- ☐1 Blood glucose monitoring -- meter
- ☐2 Lab determination (plasma)

7. Was the blood glucose measured AFTER treatment? SHAMEASD ☐1 Yes ☐2 No ☐3 Unknown

If YES,

a. By whom? SHABYWHO
- ☐1 Participant
- ☐2 Medical care personnel
- ☐3 Other

b. Record measurement ☐☐☐ mg/dl SHAMEAST
OR, if UNKNOWN, check here ⇒ ☐1 SHAUNKNO

c. Method used SHAMETHO
- ☐1 Blood glucose monitoring -- meter
- ☐2 Lab determination (plasma)

Clinic ☐☐ | Participant ID ☐☐☐☐☐ | Date of form completion (mm/dd/yyyy) ☐☐/☐☐/☐☐☐☐ | Hypoglycemic event number ☐

C. Treatment of Clinical Manifestation

8. Did the symptoms reverse without treatment? SHREVERS ☐1 Yes ☐2 No ☐3 Unknown

9. Was the participant hospitalized or treated in an emergency room or other medical facility? SHHOSPIT ☐1 Yes ☐2 No ☐3 Unknown

10. Treatment administered: (check all that apply)

a. SHTINTRA ☐1 Intravenous glucose

b. SHTGLUCA ☐1 Glucagon

c. SHTORALC ☐1 Oral carbohydrates

d. SHTOTHE ☐1 Other, describe: SHTOTHES _____

_____

D. Associated Events

11. Did any of the following occur with the hypoglycemic event described above? ☐1 Yes ☐2 No SHDEVENT

If YES, check all that apply:

a. SHDDEATH ☐1 Death

b. SHDNEURO ☐1 Neurological insult requiring hospitalization

c. SHDMYOCA ☐1 Myocardial infarction

d. SHDSTROK ☐1 Stroke

e. SHDINPAR ☐1 Injury to the participant requiring hospitalization

f. SHDINPER ☐1 Injury to another person

g. SHDPROPE ☐1 Property damage

h. SHDTRAFF ☐1 Traffic violation

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Hypoglycemic event number
☐☐	☐☐☐☐☐	☐☐/☐☐/☐☐☐☐	☐

E. Diurnal Frequency

12. Indicate the time of the onset of the episode (best estimate):

a. Indicate the period in which the episode began SHEPERIO

- ☐1 12:00 a.m. – 3:59 a.m.
- ☐2 4:00 a.m. – 7:59 a.m.
- ☐3 8:00 a.m. – 11:59 a.m.
- ☐4 12:00 p.m. – 3:59 p.m.
- ☐5 4:00 p.m. – 7:59 p.m.
- ☐6 8:00 p.m. – 11:59 p.m.
- ☐7 Unknown

b. If KNOWN, record the time ☐☐:☐☐ o'clock SHETIME

☐1 a.m. ☐2 p.m. SHEAMPM

OR, if UNKNOWN, check here ⇒ ☐1 SHEUNKNO

13. Onset of hypoglycemia occurred while participant was ☐1 Asleep ☐2 Awake SHEONSET

F. Description of the Event

14. Participant's location at onset of episode: SHFLOCA

- ☐1 Home
- ☐2 Work
- ☐3 School
- ☐4 Automobile
- ☐5 Unknown
- ☐6 Other, specify: SHFLOCAS

_____

_____

_____

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Hypoglycemic event number
☐☐	☐☐☐☐☐	☐☐/☐☐/☐☐☐☐	☐

F. Description of the Event (continued)

15. If participant was awake,

a. Were warning signs or symptoms present prior to the episode? SHFWARNI ☐1 Yes ☐2 No ☐3 Unknown

If YES,

b. Were these recognized as symptoms of hypoglycemia by the participant? ☐1 Yes ☐2 No ☐3 Unknown SHFREPAR

c. Another person? ☐1 Yes ☐2 No ☐3 Unknown SHFREPER

G. Potential Contributing Factors

16. Characterize the participant's exercise preceding the hypoglycemic event:

a. Exercise during the same four-hour period in Item 12a SHGXSAME

☐1 None
☐2 Sedentary
☐3 Moderate
☐4 Strenuous
☐5 Unknown

b. Was this unusual for this participant? SHGXSAMU ☐1 Yes ☐2 No ☐3 Unknown

c. Exercise during the previous 24 hours excluding the four-hour period in Item 12a SHGXPREV

☐1 None
☐2 Sedentary
☐3 Moderate
☐4 Strenuous
☐5 Unknown

d. Was this unusual for this participant? SHGXPREU ☐1 Yes ☐2 No ☐3 Unknown

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)	Hypoglycemic event number
☐☐	☐☐☐☐☐	☐☐/☐☐/☐☐☐☐	☐

G. Potential Contributing Factors (continued)

17. Characterize the participant's diet preceding this hypoglycemic event: (check all that apply)

a. During the same four-hour period in Item 12a

	Meal	Snack	Unknown
Missed	☐ SHG04MIM	☐ SHG04MIS	☐1 SHG04MIU
Delayed	☐ SHG04DEM	☐ SHG04DES	☐1 SHG04DEU
Ate less than usual	☐ SHG04ATM	☐ SHG04ATS	☐1 SHG04ATU

b. During the previous 24 hours excluding the four-hour period in Item 12a

	Meal	Snack	Unknown
Missed	☐ SHG24MIM	☐ SHG24MIS	☐1 SHG24MIU
Delayed	☐ SHG24DEM	☐ SHG24DES	☐1 SHG24DEU
Ate less than usual	☐ SHG24ATM	☐ SHG24ATS	☐1 SHG24ATU

18. Any alcohol or other recreational drug consumption preceding hypoglycemic event?

a. During the same four-hour period in Item 12a SHGALC04 ☐1 Yes ☐2 No ☐3 Unknown

b. During the previous 24 hours excluding the four-hour period in Item 12a SHGALC24 ☐1 Yes ☐2 No ☐3 Unknown

19. Were other potentially contributing factors present? SHGOTHE ☐1 Yes ☐2 No ☐3 Unknown

If YES, specify _____

SHGOTHES _____

_____

TINSAL-T2D Stage 2 Form STATUS
Participant Study Status

Clinic	Participant ID	Date of form completion (mm/dd/yyyy)
CLINIC	PATIENT	STCOMPDT

1. Nickname STNICKNA

2. Date of change of status or death (mm/dd/yyyy) STCHANDT

3. Staff ID STSTAFFI

*Instructions: Update this form each time the participant changes study status beginning with run-in. If coded study medications are stopped for ≥ 72 hours, complete form **MEDLOG.***

Status change information

4. Updated status STUPDATE

- 1 Withdrawal (e.g., actively and formally withdrew consent, unwilling to continue)
- 2 Deceased → *Complete **SAE Tracker** on the TINSAL-T2D website*

If withdrawal (status=1), continue. Otherwise, STOP.

5. Primary reason for withdrawal status: ***(Check one)*** STREASON

- 1 Side effects of treatment(s)
- 2 Participant discomfort with returning to study, discomfort or conflict with study staff
- 3 Study burden
- 4 Transportation
- 5 Family issues
- 6 School issues
- 7 Jail or other residential treatment facility
- 8 Safety for participant or staff (e.g., inappropriate behavior, alcohol or drug abuse)
- 9 Moved, unable to continue with TINSAL-T2D or no forwarding address
- 10 Pregnancy
- 11 Other (specify: _____ STSPECIF _____ _____)

TINSAL-T2D Stage 2 Form VISIT
Run-In, Baseline and Follow-Up Visits

VVISID

RUN=Visit 2
BAS=Visit 3
W02=Visit 4
W04=Visit 5
W08=Visit 6
W12=Visit 7
W16=Visit 8
W24=Visit 9
W36=Visit 10
W48=Visit 11
W50=Visit 12

Clinic	Participant ID	Visit ID
CLINIC	PATIENT	

1. Nickname VNICKNA ☐☐☐☐☐☐

2. Visit date (mm/dd/yyyy) VVISIDT ☐☐/☐☐/☐☐☐☐

   a. or, check here if the visit was missed: ☐1 VMISS

3. Staff ID VSTAFF ☐☐☐

4. For visit 4, W02 only, check here if phone call made ☐1 VLOC

   a. Was dose titrated? VDOSETI ☐1 Yes ☐2 No

If NO, fill out MEDLOG

Instructions: Complete this form for all participants for all run-in, baseline and follow-up visits. If a participant misses a visit, or this is for a W02 phone visit provide the information above, other than "visit date", and leave the fields below blank.

5. ***(Not applicable to Run-in, Visit 2 or W04, visit 5)*** Did the participant present to the site after an overnight fast? ☐1 Yes ☐2 No VFAST

   If NO, do not collect a blood sample. Reschedule the blood draw within 3 days. When the blood sample is collected, update this form with the date of the blood draw.

   Date of blood draw (mm/dd/yyyy) VRESCHED ☐☐/☐☐/☐☐☐☐

A. Height, Weight and Vital Signs

6. Sitting blood pressure — Systolic / Diastolic

Record BP reading 3 only if first 2 readings vary by more than 10%.

   a. BP reading 1 (after sitting 5 minutes) VSYS1 ☐☐☐/☐☐☐ VDIA1 mmHg

   b. BP reading 2 (after waiting 1 minute) VSYS2 ☐☐☐/☐☐☐ VDIA2 mmHg

   c. BP reading 3 (after waiting 1 minute) VSYS3 ☐☐☐/☐☐☐ VDIA3 mmHg

7. Heart rate VHR ☐☐☐ bpm

TINSAL-T2D Stage 2 Form VISIT
Run-In, Baseline and Follow-Up Visits

Clinic ☐☐ Participant ID ☐☐☐☐☐ Visit ID ☐☐☐

If Dinamap® is used for both BP and heart rate, record first heart rate measurement

A. Height, Weight and Vital Signs (continued)

8. Anthropometrics

For weight, record Measure 3 only if first 2 measurements are not within 0.2 kilograms.

a. Weight

VWEIGHT1 ☐☐☐.☐ kg VWEIGHT2 ☐☐☐.☐ kg VWEIGHT3 ☐☐☐.☐ kg

For height, record Measure 3 only if first 2 measurements are not within 0.5 centimeters. Record height at baseline visit only (Visit 3).

b. Height

VHEIGHT1 ☐☐☐.☐ cm VHEIGHT2 ☐☐☐.☐ cm VHEIGHT3 ☐☐☐.☐ cm

9. Examiner IDs a. BP: VBPID ☐☐☐ b. HR: VHRID ☐☐☐ c. Anthropometrics: VANTHID ☐☐☐

B. Diabetes Medication and Rescue Therapy

10. When was the last dose of study medication taken?

Date: ☐☐/☐☐/☐☐☐☐ VLASTDOD

VLASTDOT Time: ☐☐:☐☐ ☐1 AM ☐2 PM VLASTDOA

11. Is there a change in diabetes therapy other than salsalate? ☐1 Yes ☐2 No VNEWRX

If YES,

a. Reason for change: VREASON

☐1 Adjusted based on home monitoring or by PCP
☐2 Met protocol criteria for rescue therapy
☐3 Hyperglycemia
☐4 Hypoglycemia
☐5 Other (specify _____ VREASONS _____)

b. Date of change in therapy: ☐☐/☐☐/☐☐☐☐ VCHGTHDT

Clinic ☐☐ Participant ID ☐☐☐☐☐ Visit ID ☐☐☐

B. Diabetes Medication and Rescue Therapy (continued)

c. What medication is the participant currently taking?

Metformin ☐1 Yes ☐2 No VMETFO

Dose: ☐☐☐☐ mg VMETFOD

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h VMETFOF

☐7 Other (specify): ☐☐☐☐☐ VMETFOFS

Insulin secretagogue ☐1 Yes ☐2 No VINSUS

Dose: ☐☐☐☐ mg VINSUSD

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h VINSUSF

☐7 Other (specify): ☐☐☐☐☐ VINSUSFS

Insulin ☐1 Yes ☐2 No VINSUL

Type: ☐1 Glargine ☐2 NPH/Lente ☐3 Regular VINSULT

☐4 Humalog /Novalog ☐5 Ultralente ☐6 Other

Dose: ☐☐☐ total units per day VINSULD

Other ☐1 Yes ☐2 No VCHOTH

Specify: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ VCHOTHS

Dose: ☐☐☐☐ mg VCHOTHD

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h VCHOTHF

☐7 Other (specify): ☐☐☐☐☐ VCHOTHFS

Clinic	Participant ID	Visit ID
☐☐	☐☐☐☐☐	☐☐☐

C. Medication Dispensation

12. ***(Not applicable to Run-in, Visit 2)*** Number of tablets returned: ☐☐☐ tablets VTABRET

Note: If the medication dose has changed, complete Form MEDLOG.

13. ***(Not applicable to Run-in, Visit 2)*** Medication adherence rate: ☐☐☐ % VADHER

$$\frac{\text{(\# capsules dispensed - \# capsules returned) * 100}}{\text{\# of pills that should have been taken}}$$

If < 80% on baseline visit, then participant is ineligible.

a. If the participant has completed a 2-week extension of the run-in period as described in the MOP, enter the 2-week adherence rate here: ☐☐☐ % VADHER2

If < 90% during 2-week extension, then participant is ineligible.

14. ***(Not applicable to W48, Visit 11 or W50, Visit 12)***

a. Number of tablets dispensed on this visit: ☐☐☐ tablets VTABDISP

b. ***(Applicable to Run-in, Visit 2, only)*** Bottle number: ☐☐☐☐ VBOTTLE

c. ***(Not applicable to Run-in, Visit 2)*** Kit ID from which tablets were dispensed: ☐☐☐ V_KITID

TINSAL-T2D Stage 2 Form VISIT v2
Run-In, Baseline and Follow-Up Visits

VVISID

RUN=Visit 2
BAS=Visit 3
W02=Visit 4
W04=Visit 5
W08=Visit 6
W12=Visit 7
W16=Visit 8
W24=Visit 9
W36=Visit 10
W48=Visit 11
W50=Visit 12
W56=Visit 13

Clinic ☐☐ CLINIC

Participant ID ☐☐☐☐☐ PATIENT

Visit ID ☐☐☐

1. Nickname VNICKNA ☐☐☐☐☐☐

2. Visit date (mm/dd/yyyy) VVISIDT ☐☐/☐☐/☐☐☐☐

   a. or, check here if the visit was missed: ☐1 VMISS

3. Staff ID VSTAFF ☐☐☐

4. For visit 4, W02, or visit 13, W56, check here if phone call made ☐1 VLOC

   a. For visit 4, W02, was dose titrated? ☐1 Yes ☐2 No VDOESTI

   If NO, fill out MEDLOG

   b. For visit 13, W56, has tinnitus resolved? ☐1 Yes ☐2 No VTINRESO

Instructions: Complete this form for all participants for all run-in, baseline and follow-up visits. If a participant misses a visit, or this is for a W02 phone visit provide the information above, other than "visit date", and leave the fields below blank.

5. ***(Not applicable to Run-in, Visit 2 or W04, visit 5)*** Did the participant present to the site after an overnight fast? ☐1 Yes ☐2 No VFAST

   If NO, do not collect a blood sample. Reschedule the blood draw within 3 days. When the blood sample is collected, update this form with the date of the blood draw.

   Date of blood draw (mm/dd/yyyy) VRESCHED ☐☐/☐☐/☐☐☐☐

A. Height, Weight and Vital Signs

6. Sitting blood pressure Systolic / Diastolic

Record BP reading 3 only if first 2 readings vary by more than 10%.

   a. BP reading 1 (after sitting 5 minutes) VSYS1 ☐☐☐/☐☐☐ VDIA1 mmHg

   b. BP reading 2 (after waiting 1 minute) VSYS2 ☐☐☐/☐☐☐ VDIA2 mmHg

   c. BP reading 3 (after waiting 1 minute) VSYS3 ☐☐☐/☐☐☐ VDIA3 mmHg

7. Heart rate VHR ☐☐☐ bpm

If Dinamap® is used for both BP and heart rate, record first heart rate measurement

Clinic ☐☐ Participant ID ☐☐☐☐☐ Visit ID ☐☐☐

A. Height, Weight and Vital Signs (continued)

8. Anthropometrics

For weight, record Measure 3 only if first 2 measurements are not within 0.2 kilograms.

a. Weight

VWEIGHT1 ☐☐☐.☐ kg VWEIGHT2 ☐☐☐.☐ kg VWEIGHT3 ☐☐☐.☐ kg

For height, record Measure 3 only if first 2 measurements are not within 0.5 centimeters. Record height at baseline visit only (Visit 3).

b. Height

VHEIGHT1 ☐☐☐.☐ cm VHEIGHT2 ☐☐☐.☐ cm VHEIGHT3 ☐☐☐.☐ cm

9. Examiner IDs a. BP: VBPID ☐☐☐ b. HR: VHRID ☐☐☐ c. Anthropometrics: VANTHID ☐☐☐

B. Diabetes Medication and Rescue Therapy

10. When was the last dose of study medication taken?

Date: ☐☐/☐☐/☐☐☐☐ VLASTDOD

Time: ☐☐:☐☐ VLASTDOT ☐1 AM ☐2 PM VLASTDOA

11. Is there a change in diabetes therapy other than salsalate? ☐1 Yes ☐2 No VNEWRX

If YES,

a. Reason for change: VREASON

☐1 Adjusted based on home monitoring or by PCP
☐2 Met protocol criteria for rescue therapy
☐3 Hyperglycemia
☐4 Hypoglycemia
☐5 Other (specify _____ VREASONS _____)

b. Date of change in therapy: ☐☐/☐☐/☐☐☐☐ VCHGTHDT

Clinic | Participant ID | Visit ID

B. Diabetes Medication and Rescue Therapy (continued)

c. What medication is the participant currently taking?

Metformin ☐1 Yes ☐2 No VMETFO

Dose: ☐☐☐☐ mg VMETFOD VMETFOF

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h

☐7 Other (specify): ☐☐☐☐☐ VMETFOFS

Insulin secretagogue ☐1 Yes ☐2 No VINSUS

Dose: ☐☐☐☐ mg VINSUSD VINSUSF

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h

☐7 Other (specify): ☐☐☐☐☐ VINSUSFS

Insulin ☐1 Yes ☐2 No VINSUL

Type: ☐1 Glargine ☐2 NPH/Lente ☐3 Regular VINSULT

☐4 Humalog /Novalog ☐5 Ultralente ☐6 Other

Dose: ☐☐☐ total units per day VINSULD

Other ☐1 Yes ☐2 No VCHOTH

Specify: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ VCHOTHS

Dose: ☐☐☐☐ mg VCHOTHD VCHOTHF

Frequency: ☐1 QD ☐2 BID ☐3 TID ☐4 PRN ☐5 QID ☐6 Q4h

☐7 Other (specify): ☐☐☐☐☐ VCHOTHFS