## Diagnosis

1. Has the participant been diagnosed with diabetes? [ ]  Yes [ ]  No [ ]  Unknown

If YES, continue the rest of questions below (Diabetes questions)

1. Has the participant been told they have a history of high blood sugars? [ ]  Yes [ ]  No [ ]  Unknown
2. Has the participant ever been diagnosed with “pre-diabetes” (impaired fasting glucose, impaired glucose tolerance)? [ ]  Yes [ ]  No [ ]  Unknown
3. Has the participant ever been told they have a history of low blood sugars (hypoglycemia)? [ ]  Yes [ ]  No [ ]  Unknown

 If YES, please complete the “Hypoglycemia” section.

### DIABETES QUESTIONS

1. How old was the participant at diagnosis?

years months (under 21 years) or years (21 years and older)

1. Which of these was present at diagnosis? (Choose all that apply)
	1. Clinical symptoms: [ ]  Excessive thirst or urination [ ]  Weight loss (or failure to gain weight in children and adolescents) [ ]  Fatigue
	2. Laboratory diagnosis: [ ]  Elevated fasting blood sugar [ ]  Elevated random blood sugar

[ ]  Abnormal glucose tolerance testing [ ]  Elevated hemoglobin A1C [ ]  Glucose in the urine

[ ]  Any positive anti-pancreatic auto-antibody laboratory tests [ ]  Diabetic ketoacidosis

1. Was the participant hospitalized at the time of diagnosis? [ ]  Yes [ ]  No [ ]  Unknown
2. Did the participant receive insulin at the time of diagnosis? [ ]  Yes [ ]  No [ ]  Unknown
3. What type of diabetes was the participant told that they have? [ ]  Type 1 diabetes [ ]  Type 2 diabetes [ ]  Monogenic diabetes (MODY) [ ]  Mitochondrial diabetes [ ]  Gestational diabetes [ ]  Other [ ]  Unknown
	1. Did the participant have genetic testing related to diabetes? [ ]  Yes [ ]  No [ ]  Unknown
		1. If YES, what were the results?
4. If known, at diagnosis of diabetes what was the participant’s BMI category? [ ]  Underweight [ ]  Normal weight [ ]  Overweight [ ]  Obese
5. If known, what was the participant’s hemoglobin A1C at diabetes **diagnosis:** % or mmol/mol
6. If known, what is the participant’s **current** hemoglobin A1C level: % or mmol/mol
	1. If known, methodology of hemoglobin A1C level: [ ]  Point of care [ ]  Immunoassay [ ]  HPLC [ ]  Enzymatic [ ]  Other [ ]  Unknown

### BIRTH HISTORY

1. Was the participant born at term? [ ]  Yes [ ]  No [ ]  Unknown
2. If NO, how many weeks early was the participant born?
3. What was the participant’s birth weight? lbs oz OR kg
4. Did the participant’s mother have diabetes during pregnancy? [ ]  Yes, preexisting diabetes [ ]  Yes, gestational diabetes [ ]  No [ ]  Unknown

### FAMILY HISTORY

1. Does the participant have any family members (mother, father, sibling, or grandparent only) with history of diabetes? [ ]  Yes [ ]  No [ ]  Unknown

If YES, select the relation of the family member and the approximate age of onset.

1. [ ]  Mother [ ]  Father [ ]  Grandparent [ ]  Sibling
	* 1. Age of onset: [ ]  Unknown
		2. Is this individual currently on insulin? [ ]  Yes [ ]  No [ ]  Unknown
2. [ ]  Mother [ ]  Father [ ]  Grandparent [ ]  Sibling
	* 1. Age of onset: [ ]  Unknown
		2. Is this individual currently on insulin? [ ]  Yes [ ]  No [ ]  Unknown
3. [ ]  Mother [ ]  Father [ ]  Grandparent [ ]  Sibling
	* 1. Age of onset: [ ]  Unknown
		2. Is this individual currently on insulin? [ ]  Yes [ ]  No [ ]  Unknown
4. [ ]  Mother [ ]  Father [ ]  Grandparent [ ]  Sibling
	* 1. Age of onset: [ ]  Unknown
		2. Is this individual currently on insulin? [ ]  Yes [ ]  No [ ]  Unknown
5. Indicate whether the participant’s mother or father has a history of the following:
	1. Kidney disease that required dialysis or kidney transplant:

[ ]  Mother [ ]  Father [ ]  Both [ ]  Neither [ ]  Unknown

* 1. Heart attacks, heart failure or other heart problems:

[ ]  Mother [ ]  Father [ ]  Both [ ]  Neither [ ]  Unknown

* 1. Stroke: [ ]  Mother [ ]  Father [ ]  Both [ ]  Neither [ ]  Unknown
	2. High cholesterol: [ ]  Mother [ ]  Father [ ]  Both [ ]  Neither [ ]  Unknown
	3. High blood pressure: [ ]  Mother [ ]  Father [ ]  Both [ ]  Neither [ ]  Unknown

**Please note exercise information and tobacco use history are covered in the General CDEs and exercise physiology section. Information regarding nutrition is in the nutrition section.**

## Diabetes-Related Treatment History

1. Was the participant on medications to lower blood sugar **prior** to diagnosis of diabetes?

[ ]  Yes [ ]  No [ ]  Unknown

If YES,

* 1. Select the medication:

[ ]  Metformin

[ ]  GLP1RA (Examples: Liraglutide (Victoza), Exenatide (Byetta, Bydureon), Semaglutide,

Lixisenatide, Dulaglutide (Trulicity), Albiglutide (Tanzeum)

[ ]  SGLT2i (Examples: Dapagliflozin (Farxiga), Empagliflozin (Jardiance), Canagliflozin

(Invokana), Ertugliflozin (Steglatro)

[ ]  Other

### DKA AND SEVERE HYPOGLYCEMIA INFORMATION

1. **Since diagnosis** has the participant ever experienced diabetic ketoacidosis (high blood sugar plus ketones, also known as DKA) diagnosed by a doctor for which they went to either the hospital, emergency room, or another healthcare facility? [ ]  Yes [ ]  No

If YES, answer 1a-1b. If NO, skip to question 2.

* 1. If YES, # of events
	2. **In the past 12 months**, has the participant experienced diabetic ketoacidosis (high blood sugar plus ketones, also known as DKA) diagnosed by a doctor for which he/she went to either the hospital, emergency room, or another healthcare facility? [ ]  Yes [ ]  No
		1. If YES, how many times?
1. **Since diagnosis** has the participant ever experienced severe hypoglycemia that resulted in passing out, losing consciousness, or seizure? [ ]  Yes [ ]  No

If YES, answer 2a-2b.

* 1. If YES, # of events
	2. **In the past 12 months**, has the participant experienced severe hypoglycemia that resulted in passing out, losing consciousness, or seizure? [ ]  Yes [ ]  No
		1. If YES, how many times?

### HOME BLOOD GLUCOSE METER

1. What method does the participant use to check blood glucoses? [ ]  Participant does not check glucose levels at home [ ]  Fingersticks [ ]  Continuous glucose monitor (CGM)
	1. If the participant uses fingersticks, approximately how many times a day do they check their blood sugar? /day

### INSULIN USE

1. Is the participant currently on insulin? [ ]  Yes [ ]  No

If YES, complete the following:

* 1. What insulin delivery method was the participant using coming into the visit?

[ ]  Insulin pump (traditional/manual)

[ ]  Automated insulin delivery system (integrated pump/CGM)

[ ]  Injections (multiple daily injections/”basal-bolus”)

[ ]  Injections (fixed dose)

[ ]  Daily long acting only

[ ]  Fixed mix

[ ]  Injections (correction doses only)

[ ]  Injections (daily long acting/ prn corrections)

* 1. Insulin Doses: (enter average if not constant)
		1. Total daily basal insulin (or long acting) in units: [0-200] [ ]  Not used
		2. Total daily bolus insulin (or short acting) in units: [0-200] [ ]  Not used
		3. NPH: [ ]  Not used
		4. Premix: [ ]  Not used
	2. Number of missed injections or pump boluses in the past 2 weeks:
	3. If using injections, number of injections per day (enter average if not constant):
		1. Does the participant use a Pen? [ ]  Yes [ ]  No [ ]  Unknown
1. **Does the participant have any difficulty injecting insulin (using your insulin syringes, pen, or pump)?** [ ]  Yes, difficulty using syringes [ ]  Yes, difficulty using pens [ ]  Yes, difficulty using insulin pump [ ]  No
	1. If YES, what is causing the challenges using the insulin device? (Choose all that apply)

 [ ]  Decreased vision [ ]  Poor dexterity [ ]  Other, specify:

**OTHER MEDICATIONS**

1. Is the participant or has the participant previously been on any diabetes medications other than insulin? [ ]  Yes [ ]  No

If YES, please complete below and chose all that apply:

1. Metformin (biguanides) - Examples: Fortamet, Glucophage, Glumetza, Riomet

[ ]  Yes, currently [ ]  Yes, previously [ ]  No

1. Sulfonylureas - Examples: Tolbutamide (Orinase), Glimepiride (Amaryl), Glipizide (Glucotrol), Glyburide (Micronase, DiaBeta, Glynase), Chlorpropamide

[ ]  Yes, currently [ ]  Yes, previously [ ]  No

1. Thiazolidinediones (TZDs) - Examples: Pioglitazone (Actos), Rosiglitazone (Avandia)

[ ]  Yes, currently [ ]  Yes, previously [ ]  No

1. GLP-1 agonists - Examples: Liraglutide (Victoza), Exenatide (Byetta, Bydureon), Semaglutide, Lixisenatide, Dulaglutide (Trulicity), Albiglutide (Tanzeum)

[ ]  Yes, currently [ ]  Yes, previously [ ]  No

1. DPP-4 inhibitors - Examples: Sitagliptin, (Januvia), Saxagliptin (Onglyza), Alogliptin (Nesina), Linagliptin (Tradjenta)

[ ]  Yes, currently [ ]  Yes, previously [ ]  No

1. SLGT2 inhibitors - Examples: Dapagliflozin, (Farxiga), Empagliflozin (Jardiance), Canagliflozin (Invokana), Ertugliflozin (Steglatro)

[ ]  Yes, currently [ ]  Yes, previously [ ]  No

1. Other (Glinides, alpha-glucosidase inhibitors (acarbose), etc.)

[ ]  Yes, currently [ ]  Yes, previously [ ]  No

1. Combination medications

[ ]  Yes, currently [ ]  Yes, previously [ ]  No

## Diabetes-Related Health Services Utilization

1. In the last 12 months, has the participant had to use the Emergency Room? [ ]  Yes [ ]  No [ ]  Unknown

If YES, complete the following:

1. How many times did the participant go to the Emergency Room?
2. Number of times the participant went to the Emergency Room for:
3. Hypoglycemia (low blood sugars):
4. Hyperglycemia (high blood sugars):
5. Other reasons related to diabetes:
6. Reasons unrelated to diabetes:
7. In the last 12 months, has 911 been called because of the participant’s diabetes?

[ ]  Yes [ ]  No [ ] Unknown

If YES, complete the following:

1. How many times was 911 called?
2. Number of times 911 was called for:
3. Hypoglycemia (low blood sugars):
4. Hyperglycemia (high blood sugars):
5. Other reasons related to diabetes:
6. Reasons unrelated to diabetes:
7. In the last 12 months, has the participant had to use an After Hours/Urgent Care Clinic (other than an Emergency Room)? [ ]  Yes [ ]  No [ ]  Unknown

If YES, complete the following:

* 1. How many times did the participant go to the After Hours/Urgent Care Clinic?
	2. How many times did the participant go to the After Hours/Urgent Care Clinic for:
		1. Hypoglycemia (low blood sugars):
		2. Hyperglycemia (high blood sugars):
		3. Other reasons related to diabetes:
		4. Reasons unrelated to diabetes:
1. In the last 12 months, has the participant had to be admitted to the Hospital? [ ]  Yes [ ]  No [ ]  Unknown

If YES, complete the following:

1. How many times was the participant admitted to the Hospital?
2. How many times was the participant admitted to the Hospital for:
3. Hypoglycemia (low blood sugars):
	* + 1. # of days for all hypoglycemia admissions:
4. Hyperglycemia (high blood sugars):
	1. # of days for all hyperglycemia admissions:
5. Other reasons related to diabetes:
	1. # of days for all other diabetes related admissions:
6. Other reasons unrelated to diabetes:

 4. # of days for all non-diabetes related admissions:

1. In the last 12 months, has the participant seen a health care provider like a physician or nurse practitioner for an office visit? [ ]  Yes [ ]  No [ ]  Unknown

If YES, complete the following:

1. How many times has the participant seen a health care provider like a physician or nurse practitioner for an office visit for diabetes? [ ]  Unknown
2. How many times has the participant seen a health care provider like a physician or nurse practitioner for an office visit for other reasons? [ ]  Unknown
3. In the last 12 months, has the participant seen a dietician?

[ ]  Yes [ ]  No [ ]  Unknown

If YES, complete the following:

1. How many times has the participant seen a dietician? [ ]  Unknown

## Hypoglycemia

1. Has there ever been clinical concern for hypoglycemia? [ ]  Yes [ ]  No [ ]  Unknown
	1. If YES, select all that apply:

[ ]  Fasting

[ ]  Post-prandial

[ ]  Laboratory blood glucose < 50 mg/dL

[ ]  Symptomatic? If so, specify:

[ ]  Symptoms improved after feeding

1. Has the participant taken any medication for hypoglycemia? [ ]  Yes [ ]  No [ ]  Unknown
	1. If YES, what medication? [ ]  Diazoxide [ ]  Octreotide/Lanreotide [ ]  Corn starch [ ]  Other
2. Have any feeding changes been made due to hypoglycemia? [ ]  Yes [ ]  No [ ]  Unknown
	1. If YES, what change? (Choose all that apply) [ ]  Placement of a G-tube [ ]  Continuous feeds [ ]  Overnight feeds [ ]  Slower feeds [ ]  Increased calories in feeds
3. If the participant has a diagnosis of hypoglycemia, have they been told the cause?

[ ]  Ketotic hypoglycemia [ ]  Hyperinsulinism [ ]  Adrenal insufficiency [ ]  Growth hormone deficiency [ ]  Other

Recorder Signature: Date:

## General Instructions

This form is intended to obtain additional information regarding the diagnosis, treatment, and health services utilization of individuals with mitochondrial disease who also have diabetes mellitus, which represents a relatively common endocrine complication. (1) This form is based largely on questionnaires utilized by the Pediatric Diabetes Consortium.

Important note: None of the data elements included on this CRF Module are classified as Core (i.e., strongly recommended for all mitochondrial disease clinical studies to collect). (2) The data elements of the first section (Diagnosis) are considered to be Supplemental – Highly Recommended for any study focused on diabetes mellitus in mitochondrial disease. The balance of elements are considered Exploratory, based on the purposes of the particular study.

Please see the Data Dictionary for element classifications.

## Specific Instructions

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

Important note: Laboratory details can be found in the endocrine-related laboratory CRF. Physical activity details can be found in the Exercise Physiology subdomains. Other elements can be found in the Dietary Supplements CRF. For diabetes related CDEs, please refer to the Medications CRF.

It is noted that that both the pediatric and adult Newcastle Mitochondrial Disease scales include questions related to impaired endocrine function in the context of assessing related to the overall burden of endocrine disease. (3) (4)

Outside of the United States, evaluate the second set of Diabetes-Related Health Services Utilization questions (those referring to 911 calls) with respect to the direct-dial emergency number(s) applicable to the study site.

## References

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3. Elson JL, Cadogan M, Apabhai S, Whittaker RG, Phillips A, Trennell MI, Horvath R, Taylor RW, McFarland R, McColl E, Turnbull DM, Gorman GS. Initial development and validation of a mitochondrial disease quality of life scale. Neuromuscul Disord. 2013 Apr;23(4):324-9.
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