

University Animal Care Committee Standard Operating Procedure		
Document No: 7.19	Subject: Clinical Care of Non-Obese Diabetic (NOD) Mice	
Date Issued: July 26, 2012	Revision: 3	Page No: 1

Location: Queen's University

Responsibility: Principal Investigators, Research Staff, Veterinary Staff

Purpose: The purpose of this Standard Operating Procedure (SOP) is to describe treatment and animal care procedures required for Non-Obese Diabetic (NOD) mice that are raised to and maintained in a diabetic state.

Introduction and Definitions: Non-obese diabetic (NOD) mice are a model of type-1 diabetes mellitus. They are considered to be partially immune-compromised and require specific handling and care to maintain a robust health status to ensure accurate experimental results. This includes sterile caging, food, and water, as well as weekly colony weight and blood glucose checks. The age at which diabetes first develops varies between institutions and is influenced by both genetics and the environment. Typically, female NOD mice will start to develop diabetes around 10 to 14 weeks-of-age, while males have a lower incidence and develop the disease later. The incidence of disease is highest in specific pathogen-free mice.

Adult NOD mice should be tested regularly for the onset of diabetes. Specialized care for these animals will be required (once diabetic). The mice are prone to urinary tract infections and other opportunistic infections.

The husbandry techniques specific to the NOD mouse strain, as described below, are to be used in conjunction with the protocol defining Humane Interventions as described in the Queen's University SOP# 7.2 "Humane Interventions in Mice".

Abbreviations: Animal Care Services **ACS**, Principal Investigator **PI**, subcutaneous **SC**, intravenous **IV**, intraperitoneal **IP**, intramuscular **IM**, per os **PO**, per rectum **PR**, reverse osmosis **RO**, biological safety cabinet **BSC**

1. Materials:

- Sterile caging
 - Sterile food
 - Urine glucose strips or glucometer
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University Animal Care Committee Standard Operating Procedure		
Document No: 7.19	Subject: Clinical Care of Non-Obese Diabetic (NOD) Mice	
Date Issued: July 26, 2012	Revision: 3	Page No: 2

- Sterile 25 or 26 gauge needles

2. Procedures:

- Housing/Handling:
 - a. All NOD mice should be handled using sterile technique
 - b. Sterile caging including cage base, wire food hopper, cage top (standard or bottle lid), and housing igloo
 - c. Autoclaved, sterile food
 - d. Access to chlorinated water (rack-provided autowater) and/or autoclaved water bottles filled with RO (by special request only)
 - e. Wet cages should be changed.
 - Weight/Glucose Checks:
 - a. Body weight and glucose check are to be recorded for all NOD mice **at least once a week**, or more often as needed, on a sheet kept within or near the holding room or on the cage cards. It is important that all measurements be taken at the same time of day to allow for accurate trending and comparisons. Initial diabetes onset monitoring can be performed using urine glucose strips (urine) or glucometer (blood). Once diabetes is diagnosed, only blood glucose monitoring should be used.
 - b. Urine Glucose Checks:
 - Ensure urinalysis colourmetric strips (e.g., Bayer Diastix) are stored according to manufacturer's instructions and within date.
 - Sterilize BSC with 0.5% accelerated peroxide and allow to air dry.
 - Place strip over clean surface, with test pads facing up.
 - Using sterile technique: identifying the mouse, gently restrain the animal and hold over the previously sterilized BSC. Urine can be collected directly from the mouse or from the clean surface. Ensure the mouse does not come into contact with any non-sterile materials.
 - Follow the manufacturer's instructions: watch for colourmetric change indicating glycosuria.
 - If the urinalysis is positive, retest in 24 hrs. If the positive test is confirmed, measure blood glucose levels.
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University Animal Care Committee Standard Operating Procedure		
Document No: 7.19	Subject: Clinical Care of Non-Obese Diabetic (NOD) Mice	
Date Issued: July 26, 2012	Revision: 3	Page No: 3

- c. Blood Glucose Measurements:
- Blood can be collected from the mouse following SOP#7.10.3 "Tail Vein Blood Collection in Mice". Ensure a new sterile 25g or 26g needle is to be used for each mouse for tail-vein pricks and that the site is sanitized prior to blood collection. Continue to use sterile technique.
 - Follow the manufacturer's instructions for glucometer use and ensure glucometer strips are stored according to manufacturer's instructions and within date. A small drop of blood is placed on the glucometer strip mounted within the glucometer (e.g., Abbott AlphaTRAK 2). Note that a small sample or spill-over may result in an error message; strips cannot be re-used
 - Once a mouse has a blood glucose reading of 13.9 mmol/L (250 mg/dL), daily glucose checks are required. Three consecutive days with a blood glucose reading of 13.9 mmol/L or higher is indicative of a diabetic mouse.
 - Record mouse sex and age to establish and monitor incidence.
- d. Once mice are confirmed diabetic and are required to be maintained in a diabetic state as per the approved protocol
- The mice must be health **checked a minimum of twice daily** to ensure hydration (i.e. prior to the end of the work day). This includes weekends.
 - **The following care must be provided daily, including weekends:**
 - Moist chow is to be supplied and replaced daily
 - A secondary water source is provided to the cage (i.e. a water bottle and an automatic water spigot)
 - Body weight is to be recorded
 - 1mL of sterile 0.9% sodium chloride can be administered subcutaneously and must be recorded on their cage card.
- Clinical signs apparent in NOD diabetic mice include:
 - a. Weight loss
 - b. Dehydration – positive skin tent, creamy ocular discharge
 - c. Concentrated (dark coloured) urine
 - d. Sweet smelling urine
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University Animal Care Committee Standard Operating Procedure		
Document No: 7.19	Subject: Clinical Care of Non-Obese Diabetic (NOD) Mice	
Date Issued: July 26, 2012	Revision: 3	Page No: 4

- e. Abnormal posture; hunched, walking on tip toes
- f. Greasy and rough hair coat
- g. Delayed wound healing

References:

1. **Chen D, Thayer TC, Wen L, Wong FS.** 2020. Animal Models of Diabetes, Methods and Protocols. *Methods Mol Biol* **2128**:87–92.
2. **UCSF Office of Research IACUC.** 2024. "Glucose Monitoring of Urine in Rats and Mice." IACUC Standard Procedure.

SOP Revision History:

Date	New Version
July 26, 2012	SOP Created
February 28 th , 2019	Triennial Update
February 28 th , 2022	Triennial Update
March 25 th , 2026	Triennial Update. Updated monitoring and clinical signs.