Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000104: Duchenne Video Assessment
Letter of Intent

Administrative Structure:

Description of the submitter including, but not limited to, principal investigator(s), working group member(s), institutions, and contact information not contained within the cover letter.

This proposal is being submitted by Casimir, a for-profit company focused on incorporating the patient and caregiver perspective into the development of therapeutics for rare diseases. With generous support from Charley's Fund, expertise from the team of Linda Lowes from Nationwide Children's Hospital, and recruitment outreach from Parent Project Muscular Dystrophy and the Jett Foundation, Casimir is pursuing the qualification of an outcome measure for Duchenne Muscular Dystrophy. This project is being led by Mindy Leffler, MA, President and Co-Founder of Casimir, Christine McSherry, BSN, RN, CEO and Co-Founder of Casimir, and Marielle Goyette, PhD, MPH, Senior Research Scientist at Casimir.

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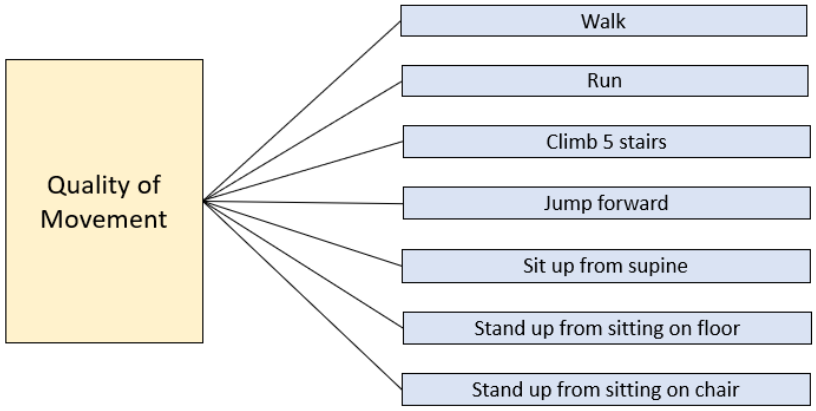
Concept(s) of Interest (COI) for Meaningful Treatment Benefit:

A description of the meaningful aspect of patient experience that will represent the intended benefit of treatment (e.g., presence/severity of symptoms, limitations in performance of daily activities).

Our concept of interest is quality of movement, measured through assessment by trained physical therapists of compensatory movements used by the patient to complete specific tasks selected as meaningful to patient life. Clinical trials predominantly assess how fast study participants can do movement tasks such as rise from the floor, go up 4 steps, or walk for 6 minutes. Only measuring speed misses the compensatory movements that study participants use to perform these tasks. Knowing whether or not a study participant uses the rail when going up 4 steps or whether a study participant pushes his hands off of his thighs to stand up are important pieces of information that are not being captured by timed testing. A study participant may move in the same amount of time but use compensatory movements to accomplish the activity. Compensatory changes are clinically meaningful and can indicate disease progression.

The movement activities that have been selected for quality of movement assessment are relevant to patients' daily lives and are potentially sensitive to change over time (**Figure 1**). Assessing the selected movement activities are a snapshot of daily life in the home environment and are reflective of patient function in daily life.

Provide a conceptual framework for the COA(s).



COU for COA Qualification:

Targeted study population including a definition of the disease and selection criteria for clinical trials (e.g., baseline symptom severity, patient demographics, comorbidities, language/culture groups)

Disease Definition:
Duchenne muscular dystrophy (DMD) is a rare, genetic disease characterized by progressive muscle degeneration and weakness.

Target Population:
This outcome measure is for use in studies enrolling patients with DMD. The DMD patient must be at least 4 years old and ambulatory. Ambulatory is defined as not needing to use a wheelchair to move from the living room to the bathroom (about 10 meters), as reported by the caregiver. Our intent is to expand the context of use to non-ambulatory DMD patients in the future.

Targeted study design and statistical analysis plan (includes the role of the planned COA in future drug development clinical trials, including the planned set of primary and secondary endpoints with hierarchy, if appropriate)

Clinical Trial Design:
This outcome measure is for use in clinical trials of drug treatments intended for use in DMD patients.

Endpoint Positioning:
This outcome measure is intended for ultimate use as an efficacy endpoint measure (ex: primary, co-primary, or secondary endpoint) in clinical trials.

Applicable study settings for future clinical trials

- ***Geographic location with language/culture groups***
- ***Other study setting specifics (e.g., inpatient versus outpatient)***

This outcome measure can be conducted in any geographic location and is designed to be conducted in a home environment. The training materials are currently in English, but they could be translated to other languages.

COA Type: Clinician Reported Outcome (ClinRO)

The COA type is best characterized as a clinician-reported outcome measure. Physical therapists will receive standardized training on scoring the video assessments; however, scoring will require a small amount of interpretation of movement characteristics from physical therapists.