Classification of Attention Task Performance Recorders Under Product Code "LQD"

Presenter
Mohua Choudhury, MS
Division of Neurosurgical, Neurointerventional & Neurodiagnostic Devices
Office of Health Technology 5-Office of Neurological and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health
Food and Drug Administration

Neurological and Physical Medicine Devices
Advisory Panel Meeting
June 3-4, 2021

Outline

- Device Description
- Indications for Use
- Regulatory History
- Clinical Background
- Literature Review
- Medical Device Reports
- Recall History
- Risks to Health & Mitigations
- Proposed Classification
- Proposed Special Controls
- FDA Questions

Device Description

- Attention task performance recorders are intended to measure reaction time (RT) in response to attention tasks. They may or may not be used to aid in the assessment or diagnosis of specific clinical conditions, most specifically attention deficit hyperactivity disorder (ADHD).
  - For general assessment of RT, the device may provide measures of both the speed of responding to stimuli and how accurately patients respond to stimuli without specific use and without providing clinical context regarding a specific disease or condition.
  - For the assessment of specific clinical conditions (e.g., ADHD), the device may additionally provide information regarding correlation with known neuropsychometric tests or aspects of cognition related to the condition of interest.
- Attention task performance recorders are typically software-based, with a test or evaluation being manually administered by a clinical end user for assessment of the symptom(s) of interest.

Indications for Use

These devices have been cleared as prescription use devices for the following representative indications for use:

- Measurement of reaction time, with tests including visual reaction speed, physical response speed, and overall motor response time.
- Provide objective measures of reaction time (speed and accuracy) to aid in the assessment of an individual's medical or psychological state.
- Provide objective measures of attention and inhibitory control to aid in the assessment of, and evaluation of treatment for, attention deficits including ADHD.
- Provide objective measures of hyperactivity, impulsivity and inattention to aid in the clinical assessment of ADHD.

Regulatory History

- Attention task performance recorders are currently a pre-amendment, unclassified device type.
- Unclassified when marketed
- Currently these devices are being regulated through the 510(k) pathway and are cleared for marketing if their intended use and technological characteristics are “substantially equivalent” to a legally marketed predicate device. Since these devices are unclassified, there is no regulation associated with the product code.
- To date, the FDA has cleared 11 devices under the LQD product code.

Clinical Background

- ADHD is a neurodevelopmental disorder characterized by three core symptom domains: inattention, hyperactivity and impulsivity.
- Clinical presentation reflects change in symptoms over time.
- Impacts children and adolescents ages 2-17 annually
  - Boys more likely to be diagnosed with ADHD in comparison to girls (12.9% compared to 5.6%).
  - 6 in 10 children have at least one other mental, emotional, or behavioral disorder (i.e., anxiety, depression, autism spectrum disorder).

- Types of ADHD:
  - **Predominantly Inattentive Presentation** (Inattention)
  - **Predominantly Hyperactive-Impulsive Presentation** (Hyperactivity and Impulsivity)
  - **Combined Presentation**: Symptoms of the above two types are equally present.

Clinical Background

- ADHD is ‘symptom complex’ – multiple causality such as genetic, biological and psychosocial influences, resulting in range of presenting behaviors
- Reliance on subjective measures leads discrepancies in diagnosis
  - Administration of interviews for data collection
  - Monitoring of response to medication
- Clinical judgment most widely accepted method of assessment
  - Gather observational information from child, parents/caregivers, and teachers
  - May use tests of behavior and neuropsychological functioning
- Use of objective measures facilitate streamlining clinical practice
  - Shorten assessment time
  - Increase diagnostic accuracy
  - Limit delays in intervention
  - Optimize treatment

Literature Review

- A systematic literature review was conducted in an effort to gather any published information regarding the safety and effectiveness of attention task performance recorders under product code “LQD.”
- Literature searches were conducted to identify any relevant articles published between January 1, 2010, and December 31, 2020.
- The searches were limited to publications in English and excluded conference proceedings and abstracts.
- The searches yielded 346 initial literature references. After duplicate articles were removed, the literature search of the above electronic databases yielded 241 literature references.
- A total of 42 published literature references, covering 41 studies, were determined to be relevant to the safety and/or effectiveness of attention task performance recorders.

Literature Review – Safety Assessment

- Search methodology did not identify literature reporting on adverse events related with the use of attention task performance recorders.

Literature Review – Effectiveness Assessment

- Search identified the following:
  - 13 studies evaluating reaction time (RT)
  - 2 studies evaluating the use of the Fagan Test as a cognitive screening tool
  - 25 studies evaluating their use to aid in the clinical assessment of ADHD or in the evaluation of treatment interventions in patients with ADHD
  - 1 study evaluating the clinical utility of attention task performance recorders for diagnosing and monitoring ADHD in children

Literature Review – Effectiveness Assessment

- Studies evaluating reaction time:
  - DANA can measure differences in measures of RT reliably
  - Greater uncertainty for Dynavision to measure RT reliably
- Studies evaluating use as cognitive screening tool:
  - Conflicting findings for Fagan Test to discriminate normal vs. abnormal cognitive skills
- Studies evaluating aiding in clinical assessment of ADHD:
  - Both Gordon Diagnostic System (GDS) and QBTest had greater accuracy when combined with other rating scales
  - QBTest had good convergent and discriminant validity
- Studies evaluating aiding in the assessment of treatment interventions of ADHD:
  - QbTest able to capture statistically significant improvement in QbTest scores measuring core ADHD symptoms in studies evaluating traditional pharmacological interventions
  - Tests of Variables of Attention (T.O.V.A.) demonstrated limited sensitivity to medication effects and group-based differences in objective measures of RT post-intervention

Literature Review – Summation

- Did not identify studies reporting adverse events related to use of an attention task performance recorder itself
- Heterogeneity of use of products included in LQD product code limits ability to draw conclusions regarding effectiveness
- Other limitations in drawing conclusions regarding effectiveness due to:
  - Studies' sample size
  - Generalizability of OUS study results to US population
  - Limitations associated with use and interpretation of rating scales
  - Limitations associated with adult self-report

Medical Device Reports

- Medical Device Reporting (MDR): the mechanism for the FDA to receive significant medical device adverse events from:
  - mandatory reporters (manufacturers, importers and user facilities)
  - voluntary reporters (health care professionals, patients, consumers)

Medical Device Reports

- MDR reports can be used effectively to:
  - Establish a qualitative snapshot of adverse events for a specific device or device type
  - Detect actual or potential device problems used in a “real world” setting/environment, including:
    - rare, serious, or unexpected adverse events
    - adverse events that occur during long-term device use
    - adverse events associated with vulnerable populations
    - off-label use
    - user error

Medical Device Reports

- Limitations
  - Under reporting of events
  - Potential submission of incomplete, inaccurate, untimely, unverified, or biased data
  - Incidence or prevalence of an event cannot be determined from this reporting system alone
  - Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report
  - MAUDE data does not represent all known safety information for a reported medical device

Medical Device Reports

- MAUDE (Manufacturer And User Facility Device Experience) Database reviewed for product code “LQD” (not time restricted):
  - No Medical Device Reports.

Recall History

- The Medical Device Recall database contains medical device recalls classified since November 2002.
- Since January 2017, it may also include correction or removal actions initiated by a firm prior to review by the FDA.
- The status is updated if the FDA identifies a violation and classifies the action as a recall and again when the recall is terminated.
- FDA recall classification (resulting in the posting date) may occur after the firm recalling the medical device product conducts and communicates with its customers about the recall.

Recall History

- Medical Device Recall Database reviewed for product code “LQD” (not time restricted):
  - No Recalls

Risks and Mitigations

Intended Use Category 1: Intended to Measure RT and Associated Patient Performance in Response to Attention Tasks Only

Risks to Health and Descriptions/Examples for Attention Task Performance Recorders Intended to Measure Reaction Time and Associated Patient Performance in Response to Attention Tasks, Without Aiding in Assessment or Diagnosis

Identified Risk	Description/Examples
Patient discomfort (e.g., visual or mental fatigue)	• Use of the devices can cause patient discomfort, such as visual or mental fatigue.
Incorrect or inaccurate measurements of reaction time or other attention tasks	• Use of the devices can result in incorrect or inaccurate measurements of reaction time or other attention tasks based on associated patient performance

Risks and Mitigations

Intended Use Category 2: Intended to Aid in Assessment or Diagnosis of Specific Diseases or Conditions

Risks to Health and Descriptions/Examples for Attention Task Performance Recorders Intended to Aid in Assessment or Diagnosis of Specific Diseases or Conditions

Identified Risk	Description/Examples
Patient discomfort (e.g., visual or mental fatigue)	• Use of the devices can cause patient discomfort, such as visual or mental fatigue.
Incorrect or inaccurate results leading to inaccurate assessment or delayed diagnosis, both of which could result in inappropriate therapy or delay in treatment	• A false positive result means that the device indicates the patient has the clinical condition or disease of interest, such as ADHD or be at risk of cognitive impairment, when in fact none is present. • A false negative result means that the device indicates the patient does not have the clinical condition or disease of interest, such as ADHD or be at risk of cognitive impairment, when in fact the clinical condition or disease is present.

Proposed Split Classification

882.1490 Attention task performance recorder.

(a) *Identification*.
An attention task performance recorder is a device intended to measure reaction time and associated patient performance in response to attention tasks. The device may or may not be used to aid in the assessment of specific clinical conditions.

Proposed Special Controls

(b) *Classification.*

(1) Class II (special controls), when intended to measure reaction time and associated patient performance in response to attention tasks only without aiding in assessment or diagnosis

1. The technical parameters of the device's hardware and software must be fully characterized and be accompanied by appropriate non-clinical testing:
    a) Hardware specifications must be provided. Appropriate verification, validation and hazard analysis must be performed, including applicable electrical safety testing.
    b) Software, including any proprietary algorithm(s) used by the device to measure reaction time and output other measures of attention, associated activities and related task performance, must be described in detail in the Software Requirements Specification (SRS) and Software Design Specification (SDS). Appropriate software verification, validation and hazard analysis must be performed.
2. Non-clinical device performance evaluation must demonstrate accurate and precise measurement of patient reaction times in response to task stimuli.
3. Labeling must include:
    a) A warning that the device is intended to aid in patient assessment or diagnosis by a trained physician and is not intended for stand-alone use.
    b) Any instructions that technicians must convey to patients regarding safe and effective administration of the specific tasks and collection of task performance data.

Proposed Special Controls

(b) *Classification.*

(2) Class II (special controls), when intended to measure reaction time and associated patient performance in response to attention tasks **for the aid in assessment or diagnosis of specific diseases or conditions:**

1. **Clinical device performance evaluation must validate that the device outputs accurately and precisely assess patient symptomology associated with the specific disease or condition for which the device is intended to assess or diagnose. The testing must:**
    - **a) Evaluate agreement between device output and patient symptomology.**
    - **b) Evaluate device test-retest reliability.**
    - **c) Describe construction of any normative or reference database, which includes the following:**
        - **i. How the clinical work-up was completed to define the reference population, including the establishment of inclusion and exclusion criteria.**
        - **ii. Statistical methods and model assumptions used.**
2. The technical parameters of the device's hardware and software must be fully characterized and be accompanied by appropriate non-clinical testing:
    1. Hardware specifications must be provided. Appropriate verification, validation and hazard analysis must be performed, including applicable electrical safety testing.
    2. Software, including any proprietary algorithm(s) used by the device to measure reaction time and output other measures of attention, associated activities and related task performance, must be described in detail in the Software Requirements Specification (SRS) and Software Design Specification (SDS). Appropriate software verification, validation and hazard analysis must be performed.
3. Non-clinical device performance evaluation must demonstrate accurate and precise measurement of patient reaction times in response to task stimuli.

Proposed Special Controls

(b) *Classification.*

(2) Class II (special controls), when intended to measure reaction time and associated patient performance in response to attention tasks **for the aid in assessment or diagnosis of specific diseases or conditions**

4. The labeling must include:
   - **a) A summary of any clinical testing conducted to demonstrate that the device outputs accurately and precisely assess patient symptomology associated with the specific disease or condition for which the device is intended to assess or diagnose. The summary of testing must include the following:**
     - **i. Agreement between device output and patient symptomology.**
     - **ii. Device test-retest reliability.**
     - **iii. A description of any normative or reference database, which includes the following:**
       1. **How the clinical work-up was completed to define the reference population, including the establishment of inclusion and exclusion criteria.**
       2. **How reference values will be reported to the user.**
       3. **Representative screenshots and reports that will be generated to provide the user results and reference data.**
       4. **Statistical methods and model assumptions used.**
       5. **Whether or not the database was adjusted due to differences in age, gender, or other factors.**
   - b) A warning that the device is intended to aid in patient assessment or diagnosis by a trained physician and is not intended for stand-alone use.
   - c) Any instructions that technicians must convey to patients regarding safe and effective administration of the specific tasks and collection of task performance data.

U.S. FOOD & DRUG ADMINISTRATION

Thank You

Questions to Panel - LQD

Mohua Choudhury, Lead Reviewer, MS, OHT5

Question 1 to Panel

FDA has identified the following risks to health for attention task performance recorders intended to measure reaction time and associated patient performance in response to attention tasks (intended use category 1):

Risks to Health and Descriptions/Examples for Attention Task Performance Recorders Intended to Measure Reaction Time and Associated Patient Performance in Response to Attention Tasks, Without Aiding in Assessment or Diagnosis

Identified Risk	Description/Examples
Patient discomfort (e.g., visual or mental fatigue)	• Use of the devices can cause patient discomfort, such as visual or mental fatigue.
Incorrect or inaccurate measurements of reaction time or other attention tasks	• Use of the devices can result in incorrect or inaccurate measurements of reaction time or other attention tasks based on associated patient performance

Question 1 to Panel

FDA has identified the following risks to health for attention task performance recorders intended aid in assessment or diagnosis of specific diseases or conditions (intended use category 2).

Risks to Health and Descriptions/Examples for Attention Task Performance Recorders Intended to Aid in Assessment or Diagnosis of Specific Diseases or Conditions

Identified Risk	Description/Examples
Patient discomfort (e.g., visual or mental fatigue)	• Use of the devices can cause patient discomfort, such as visual or mental fatigue.
Incorrect or inaccurate results leading to inaccurate assessment or delayed diagnosis, both of which could result in inappropriate therapy or delay in treatment	• A false positive result means that the device indicates the patient has the clinical condition or disease of interest, such as ADHD or be at risk of cognitive impairment, when in fact none is present. • A false negative result means that the device indicates the patient does not have the clinical condition or disease of interest, such as ADHD or be at risk of cognitive impairment, when in fact the clinical condition or disease is present.

Question 1 to Panel

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of attention task performance recorders under product code “LQD.” In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these attention task performance recorders.

Question 2 to Panel

- Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:
  - insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or that application of special controls would provide such assurance, AND
  - the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.
- A device should be Class II if:
  - general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness, AND
  - there is sufficient information to establish special controls to provide such assurance.

Question 2 to Panel

- A device should be Class I if:
  - general controls are sufficient to provide reasonable assurance of the safety and effectiveness, OR
  - insufficient information exists to:
    - determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness, OR
    - establish special controls to provide such assurance, BUT
      - is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, AND
      - does not present a potential unreasonable risk of illness or injury.

Question 2 to Panel

FDA believes general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness and sufficient information exists to establish special controls to adequately mitigate the risks to health and provide reasonable assurance of device safety and effectiveness for this device type.

As such, FDA believes that Class II is the appropriate classification for attention task performance recorders. Following are risk/mitigation tables, which outline the identified risks to health for this device type and the recommended controls to mitigate the identified risks, delineated by intended use:

Table 5: Summary of Risks to Health and Proposed Special Controls for Attention Task Performance Recorders Intended to Measure Reaction Time and Associated Patient Performance in Response to Attention Tasks, Without Aiding in Assessment or Diagnosis

Identified Risk	Recommended Mitigation Measure
Patient discomfort (e.g., visual or mental fatigue)	• Labeling
Incorrect or inaccurate measurements of reaction time or other attention tasks	• Non-clinical performance testing • Software verification, validation, and hazard analysis • Labeling

Question 2 to Panel

FDA believes general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness and sufficient information exists to establish special controls to adequately mitigate the risks to health and provide reasonable assurance of device safety and effectiveness for this device type.

As such, FDA believes that Class II is the appropriate classification for attention task performance recorders. Following are risk/mitigation tables, which outline the identified risks to health for this device type and the recommended controls to mitigate the identified risks, delineated by intended use:

Table 6: Summary of Risks to Health and Proposed Special Controls for Attention Task Performance Recorders Intended to Aid in Assessment or Diagnosis of Specific Diseases or Conditions

Identified Risk	Recommended Mitigation Measure
Patient discomfort (e.g., visual or mental fatigue)	• Labeling
Incorrect or inaccurate results leading to inaccurate assessment or delayed diagnosis, both of which could result in inappropriate therapy or delay in treatment	• Clinical performance testing • Non-clinical performance testing • Software verification, validation, and hazard analysis • Labeling

Question 2a to Panel

Please discuss whether the identified special controls appropriately mitigate the identified risks to health for attention task performance recorders *intended to measure reaction time and associated patient performance in response to attention tasks only, without aiding in assessment or diagnosis*. Please also discuss whether additional or different special controls are recommended.

Proposed Special Controls

1. The technical parameters of the device's hardware and software must be fully characterized and be accompanied by appropriate non-clinical testing:
    a) Hardware specifications must be provided. Appropriate verification, validation and hazard analysis must be performed, including applicable electrical safety testing.
    b) Software, including any proprietary algorithm(s) used by the device to measure reaction time and output other measures of attention, associated activities and related task performance, must be described in detail in the Software Requirements Specification (SRS) and Software Design Specification (SDS). Appropriate software verification, validation and hazard analysis must be performed.
2. Non-clinical device performance evaluation must demonstrate accurate and precise measurement of patient reaction times in response to task stimuli.
3. The labeling must include:
    a) A warning that the device is intended to aid in patient assessment or diagnosis by a trained physician and is not intended for stand-alone use.
    b) Any instructions that technicians must convey to patients regarding safe and effective administration of the specific tasks and collection of task performance data.

Question 2b to Panel

Please discuss whether the identified special controls appropriately mitigate the identified risks to health for attention task performance recorders *intended to measure reaction time and associated patient performance in response to attention tasks for the aid in assessment or diagnosis of specific diseases or conditions*. Please also discuss whether additional or different special controls are recommended.

Proposed Special Controls

1. **Clinical device performance evaluation must validate that the device outputs accurately and precisely assess patient symptomology associated with the specific disease or condition for which the device is intended to assess or diagnose. The testing must:**
    - **a) Evaluate agreement between device output and patient symptomology.**
    - **b) Evaluate device test-retest reliability.**
    - **c) Describe construction of any normative or reference database, which includes the following:**
        - **i. How the clinical work-up was completed to define the reference population, including the establishment of inclusion and exclusion criteria.**
        - **ii. Statistical methods and model assumptions used.**
2. The technical parameters of the device's hardware and software must be fully characterized and be accompanied by appropriate non-clinical testing:
    - a) Hardware specifications must be provided. Appropriate verification, validation and hazard analysis must be performed, including applicable electrical safety testing.
    - b) Software, including any proprietary algorithm(s) used by the device to measure reaction time and output other measures of attention, associated activities and related task performance, must be described in detail in the Software Requirements Specification (SRS) and Software Design Specification (SDS). Appropriate software verification, validation and hazard analysis must be performed.
3. Non-clinical device performance evaluation must demonstrate accurate and precise measurement of patient reaction times in response to task stimuli.

Question 2b to Panel

Please discuss whether the identified special controls appropriately mitigate the identified risks to health for attention task performance recorders *intended to measure reaction time and associated patient performance in response to attention tasks for the aid in assessment or diagnosis of specific diseases or conditions*. Please also discuss whether additional or different special controls are recommended.

4. The labeling must include:
   - **a) A summary of any clinical testing conducted to demonstrate that the device outputs accurately and precisely assess patient symptomology associated with the specific disease or condition for which the device is intended to assess or diagnose. The summary of testing must include the following:**
     - **i. Agreement between device output and patient symptomology.**
     - **ii. Device test-retest reliability.**
     - **iii. A description of any normative or reference database, which includes the following:**
       1. **How the clinical work-up was completed to define the reference population, including the establishment of inclusion and exclusion criteria.**
       2. **How reference values will be reported to the user.**
       3. **Representative screenshots and reports that will be generated to provide the user results and reference data.**
       4. **Statistical methods and model assumptions used.**
       5. **Whether or not the database was adjusted due to differences in age, gender, or other factors.**
   - b) A warning that the device is intended to aid in patient assessment or diagnosis by a trained physician and is not intended for stand-alone use.
   - c) Any instructions that technicians must convey to patients regarding safe and effective administration of the specific tasks and collection of task performance data.

Question 3 to Panel

Please discuss whether you agree with FDA's proposed classification of Class II with special controls for attention task performance recorders. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

End of Panel Questions for Product Code “LQD”

Mohua Choudhury, Lead Reviewer, MS, OHT5