FDA Executive Summary

Prepared for the June 3-4, 2021 Meeting of the Neurological Devices Panel

Classification of Plunger-Like Joint Manipulators

Product Code: LXM

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1. Introduction

Per Section 513(b) of the Food, Drug, and Cosmetic Act (the Act), the Food and Drug Administration (FDA) is convening the Neurological Devices Advisory Panel (the Panel) for the purpose of obtaining recommendations regarding the classification of plunger-like joint manipulators, a pre-amendments device type which remains unclassified. Specifically, the FDA will ask the Panel to provide recommendations regarding the regulatory classification of plunger-like joint manipulators under product code "LXM". The device names and associated product codes are developed by the Center for Devices and Radiological Health (CDRH) in order to identify the generic category of a device for FDA. While most of these product codes are associated with a device classification regulation, some product codes, including "LXM" remain unclassified.

FDA is holding this Panel meeting to obtain input on the risks to health and benefits of plunger-like joint manipulators under product code "LXM." The Panel will discuss whether plunger-like joint manipulators under product code "LXM" should be classified into class II (subject to General and Special Controls). If the Panel believes that classification into Class II is appropriate for plunger-like joint manipulators under product code "LXM," the Panel will also be asked to discuss appropriate controls that would be necessary to mitigate the risks to health.

1.1 Current Regulatory Pathways

Plunger-like joint manipulators are a pre-amendment, unclassified device type. This means that this device type was marketed prior to the Medical Device Amendments of 1976 but was not classified by the original classification panels. 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.

1.2 Device Description

Plunger-like joint manipulators are intended to be used by licensed chiropractors, medical doctors, and other licensed health care professionals for the external analysis and adjustment of the spinal column and/or extremities.

Most of the cleared plunger-like joint manipulators are handheld electromechanical instruments that are either AC or battery powered. The power generated charges a solenoid, which in turn generates a thrust force that is delivered to the patient via a plunger attached to a metal stylus.

Other plunger-like joint manipulators comprise of an actuator/electronic control and positioning stand. These devices also contain a release mechanism that prevents excessive pressure being applied to the patient.

For both handheld and freestanding plunger-like joint manipulators, the patient is positioned on the table and the chiropractor positions the stylus against the desired region of the vertebra. The thrust force being delivered to the patient can be adjusted and controlled by clutches and tension knobs or by adjusting the capacitor's voltage.

2. Regulatory History

The Precision Spinal Adjuster Model 115 manufactured by Kinetic Technology Inc. was the first LXM device cleared on April 26, 1988. The sponsor cited substantial equivalence to the Pettibon Precision Cervical Vertebrae Adjusting Instrument, a pre-amendments device which was distributed prior to 1976. To date, the FDA has cleared thirty plunger-like joint manipulators under product code LXM.

Table 1: 510(k) clearances for plunger-like joint manipulators under product code "LXM"

510(k) Number	Trade Name	Sponsor
K870910	Precision Spinal Adjuster Model 115	Kinetic Technology Inc.
K922692	Kinetic Technology Pocket Precision Adjustor	Kinetic Technology Inc.
K922693	Kinetic Technology Precision Adjustor Model SHLCP-1	Kinetic Technology Inc.
K922694	Kinetic Technology Precision Adjustor Model SHLCP-4	Kinetic Technology Inc.
K922695	Kinetic Technology Precision Adjustor Mod. SHLCP-5	Kinetic Technology Inc.
K930431	Arthrostim Manipulator	Freeman Procedure Seminars
K940085	Force Recording and Analysis System Model 01	Sense Technology Inc.
K944369	New-Stim Spinal Adjustment Instrument	Lawrence E. Newsum DC
K946258	Model 8000 Atlas C-1 Orthogonal Adjusting Instrument	Spinalight Inc.
K950646	Integrator	Moyco Union Broach Div. Moyco Technologies Inc.
K951217	Atlas Orthogonal Percussion Instrument	Sweat Chiropractic Clinic
K955540	Hand Held Atlas Instrument	Spinalight Inc.
K962239	Smart Adjuster (SA201)	Sigma
K973506	Activator II	Activator Methods Inc.

K973914	Sense Technology Inc. FRAS Sense Technology Inc. Pulstar	Sense Technology Inc.
K974376	JTECH Adjuster Reflex Gun	J-Tech Medical Inc.
K001476	Torque Instrument Model 8500	Spinalight Inc.
K003185	FS Activator III	Activator Methods International Ltd
K010851	Harrison Hand Held Adjusting Instrument	Harrison CBP Seminars
K021238	Frye Adjusting Instrument	Frye Health Systems
K023462	Impulse-Adjusting Instrument CBP Adjusting Instrument Neuromechanical Adjusting Instrument Models 2003	Neuromechanical Innovations LLC
K050428	Technology-Assisted Micro-Mobilization and Reflex Stimulator (Tamars)	Advanced Spinal Technologies Inc.
K060043	Khan Kinetic Treatment Device (KKT-M1)	Optima Health Solutions International Inc.
K072519	Activator V Spinal Adjusting Instrument	Activator Methods International LTD.
K080261	Impulse iQ Adjusting Instrument	Neuromechanical Innovations LLC
K082218	Max Adjusting Instrument	Manna Omni International Inc.
K112606	Activator V-E	Activator Methods International LTD.
K130666	Khan Kinetic Treatment (KKT-M2)	Optima Health Solutions International Corporation
K160278	VSTAAR Adjuster	Spinal Acoustics LLC
K172536	Atlas Percussion Adjusting Instrument	Spinalight Inc

3. Indications for Use

The Indications for Use (IFU) statement identifies the condition and patient population for which a device should be appropriately used.

The majority of IFU statements for plunger-liked joint manipulators refer to chiropractic adjustment or manipulation without identifying a specific disease or condition to be treated. Almost all specify targeting vertebrae or joints, although ligaments and soft tissues are also addressed. The devices listed above have been cleared for either over-the-counter (OTC) use or for prescription (Rx) use.

Representative IFU statements for plunger-like joint manipulators under product code "LXM" cleared in the 510(k)s noted in Table 1 are as follows:

- The device is intended for chiropractic adjustment.
- The device is intended for spinal subluxation, or the manipulation of spinal joints (facet joints).
- The device is intended for chiropractic adjustment of the spine and extremities.
- The device is intended for chiropractic adjustment, mobilization, or manipulation of the musculoskeletal joints of the spine and/or extremities or for soft-tissue musculoskeletal mobilization.
- The device is intended to stimulate segments of the cervical spine, thoracic spine and lumbar spine as well as the sacrum, ilium and extremities.

4. Clinical Background

4.1 Disease Characteristics

Acute and chronic musculoskeletal pain can be the result of various underlying problems including muscle strain, sprain, overuse syndromes, tendinopathies and arthritis. Goals of manipulation include symptom reduction through passive movement of the affected and adjacent areas.

Spinal manipulation is a form of manual therapy that involves the deliberate high-velocity, passive movement of a joint in the spine or periphery and may also be referred to as spinal adjustment. Although there is no convincing evidence showing a mechanism underlying the benefit of spinal manipulation, several hypotheses have been proposed including: neurophysiologic stimulation that causes pain inhibition, alteration of pain-related reflexes and central pathways, relaxation of tight muscles by stretching, and disruption of adhesions.

Manipulation or adjustments can be considered appropriate treatments for some types of musculoskeletal pain in the neck, back, shoulders and in some headache syndromes. Sometimes devices are employed to assist in performing the desired manipulation.

4.2 Patient Outcomes

Data for the efficacy of spinal manipulation is limited. Reports on serious adverse events related to spinal manipulation in general range from 1 per 100,000 to 1 per 6 million.[8] These events include: intravertebral disk herniation, cauda equina syndrome, vertebrobasilar occlusion or dissection, and carotid dissection. Patients at higher risk of serious events secondary to manipulation include: those with a history of artery dissection, vasculopathies, recent trauma to the neck, stroke or transient ischemic attack (TIA), Ehlers-Danlos syndrome and other hypermobility syndromes, bleeding disorders and anticoagulation treatment, inflammatory spondyloarthropathy, osteoporosis, Down syndrome and upper cervical instability.

4.3 Currently Available Treatment

Spinal manipulation can be performed manually, with or without the use of a device to assist in achieving movement. Alternatives to manipulation in the treatment of musculoskeletal pain include: heating or cooling, bracing, therapeutic exercise, topical analgesics, and injection of local anesthetics. Oral medication options for treatment include: non-steroidal anti-inflammatory medications, acetaminophen, muscle relaxants including: methocarbamol, cyclobenzaprine, carisoprodol and metaxalone.

4.4 Risks

FDA has identified the following risks to health associated with plunger-like joint manipulators:

Table 2: Risks to Heath and Descriptions/Examples for Plunger-Like Joint Manipulators

Identified Risk	Description/Examples
Adverse tissue reaction	This can result from use of device materials that are not biocompatible.
Electric shock or burn	This can result from electrical failure or malfunction.
Pain	This risk could be due to a mechanical, electrical or software malfunction causing device failure. Types of pain include neck pain, radiating pain, and mid-back pain.
Discomfort	This risk can be caused by a mechanical, electrical, or software malfunction causing device failure. Types of discomfort include headache, fatigue, dizziness, stiffness, mild soreness, arm weakness, and arm numbness.
Tissue injury	This risk could be due to a mechanical, electrical or software malfunction causing device failure. An example of tissue injury includes bruising from excessive force or pressure.

The Panel will be asked whether this list is a complete and accurate list of the risks to health presented by plunger-like joint manipulators under product code "LXM" and whether any other risks should be included in the overall risk assessment of the device type.

5. Literature Review

5.1 Methods

A systematic literature review (SLR) was conducted to gather any published literature regarding the safety and effectiveness of plunger-like joint manipulators that are regulated under the product code "LXM". Online literature searches were performed in two electronic databases (Embase and PubMed). Appendix A contains a list of all search terms and filters utilized for Embase and PubMed. The search was limited to human clinical studies published in the English language, with publication dates between April 27, 2010 and December 31, 2020. Database filters were used to exclude non-original human clinical studies such as: conference abstracts/proceedings, commentaries, and editorials.

An initial search was performed on April 27, 2020, using publication dates between April 27, 2010 and April 26, 2020. A supplementary search was performed on March 19, 2021, to capture any additional articles published between April 26, 2020 and December 31, 2020. Thirty-two additional articles were found in the supplemental search. The flow diagram in Appendix B represents the total number of articles and exclusion criterium obtained from both searches.

5.2 Results

The search yielded 561 initial literature references. After duplicate articles were removed between databases, a total of 548 articles remained. Following a review of the titles and abstracts, a total of 9 articles remained for full-text review. Of these, 7 articles were determined to be relevant to the safety and effectiveness of plunger-like joint manipulators (Appendix B). The number of each excluded criterium is also summarized in the flow diagram in Appendix B.

The studies retained by the literature search evaluated plunger-like joint manipulators for the treatment of neck pain, including: conditions related to neck pain, i.e., referred shoulder pain of neck origin and neck pain with concomitant dizziness, and for low back pain. All the studies involved application of the plunger-like joint manipulator device to the cervical, thoracic or lumbar spine compared to an alternative treatment and/or control treatment or compared to a placebo/sham. The seven studies identified for inclusion in the evidence assessment were conducted in the following countries: Australia[2,3,4] (3), United States[6,7] (2), and Switzerland[5] and UK[1] (1 each). Of the seven studies, six were randomized controlled trials (RCTs)[1-5, 7] and one was a prospective observational cohort study[6]. Two of the RCTs utilized a placebo/sham control and were double-blinded[3,4].

For the indication of neck pain or conditions associated with neck pain, 120 patients were treated in the plunger-like joint manipulator device group, and 148 combined patients in the alternative treatment, control or sham/placebo groups[1,2,3,4,5]. For the indication of low back pain, there were 88 patients in the plunger-like joint

manipulator device group, and 111 patients combined in the manual therapy (n=76)[6,7] and usual medical care control group (n=35)[7].

The sample size for the individual studies ranged from 5 to 65 subjects in the plunger-like joint manipulator group, and from 5 to 60 in the alternative treatment or control groups. The age of the subjects for the plunger-like manipulator group ranged from a mean of 25 years to 74 years based on the six studies that reported age solely as a mean[1, 2, 4, 5, 6, 7]. The age of the subjects in the comparison groups ranged from a mean of 24 years to 74 based on the six studies reporting mean age by group. In the six studies that reported gender for each group, 103 subjects treated with the plunger-like joint manipulator device were females (103/203 = 50.7%) and 100 were male (100/203= 49.3%)[1,2,3,4,6,7]. For control and alternative treatment groups combined, 94 subjects were females (94/196=48%) and 102 were male (102/196=52%)[1,2,3,4,6,7]. In one study, only combined demographics are reported, with a mean age for manual and mechanical assisted manipulation groups of 50.5 years, and with 8 females (8/10=80%) and 2 males (2/10=20%) treated[5].

5.3 Adverse Events Associated with Plunger-Like Joint Manipulators

Treatment of Neck Pain

Of the five studies for treatment of neck pain, three studies specifically identified the collection of adverse events as part of the study objectives and/or study methods[1,2,4] and two studies aimed at effectiveness did not specify methods for collecting adverse events[3,5]. One study reported a lower adverse event rate in the device group compared to the alternative intervention and inactive control groups (4.5% for the plunger-like joint manipulator group compared to 4.8% for the manual manipulator group and 18.2% for the stretching only control group, respectively)[2]; and two reported a higher adverse event rate in the device group compared to alternative treatment groups (43.8% for the plunger-like joint manipulator group compared to 25% and 26.7% for manual manipulation and mobilization groups, respectively)[1] and compared to a sham control (33% compared to 20%)[4]. The other two studies reported no adverse events for the plunger-like joint manipulator or comparison group or placebo[3,5]. In all but one study for treatment of neck pain, patients could not be blinded to the treatment due to the clicking sound from the device.

A total of 26 adverse events were reported in the plunger-like joint manipulator group, including neck pain (n=9), radiating pain (5), arm weakness (1), arm numbness (1), headache (4), fatigue (3), and dizziness (1), mid-back pain (1), and stiffness, mild soreness, or pain during neck movement. The same types of adverse events were reported in the comparison groups other than arm weakness, arm numbness and mid-back pain, for which there were no reports in the comparison groups and one report of each in the plunger-like joint manipulator group. Adverse events of increased neck pain and headache were observed in both the plunger-like joint manipulator and sham groups[4]. All events across studies and groups were mild and transient.

Treatment of Low Back Pain

Two studies evaluated the plunger-like joint manipulator (Activator instrument) for treatment of low back pain (LBP)[6,7]. Both studies were aimed at comparing effectiveness between mechanical manipulation and alternative treatment and did not include a specific objective for safety or methods for collecting adverse events. In one study, the authors reported an absence of adverse events[7]. In the other study, an observational cohort study, the authors did not report on adverse events[6].

5.4 Effectiveness Associated with Plunger-Like Joint Manipulators

Treatment of Neck Pain

Five studies, all RCTs, evaluated plunger-like joint manipulators for treatment of neck pain or conditions related to neck pain, including: shoulder pain of cervical origin and neck pain with concomitant dizziness[1,2,3,4,5]. The plunger-like joint manipulator was compared to manual manipulation in three studies[1,2,5,] and additionally to a mobilization group in one study[1]. In one study, the plunger-like joint manipulator device was also compared to an inactive control[2] and in two studies, the plunger like joint manipulator was compared to a placebo or sham[3,4]. Study populations included patients with non-specific or mechanical neck pain, various duration and history of neck pain (i.e., acute, subacute or chronic with various prior treatments), and various degree of pain. Treatment involved manipulation of either the cervical or thoracic spine. In these five studies, 120 patients were treated in the plunger-like joint manipulator device group, and 148 patients combined in the alternative treatment, stretching inactive control or placebo/sham groups.

In four of five studies, the plunger-like joint manipulator group was found to be statistically and/or clinically significant for improving pain based on a variety of pain intensity measurements compared to baseline[1,3,4,5]. In the remaining study[2], there was no statistically or clinically significant reduction in pain from baseline in the plunger-like manipulator group. There were no statistically significant between-group differences for the plunger-like joint manipulator compared to alternative interventions or to inactive controls reported in any of these studies.

In one study, comparing the Activator device to manual manipulation and mobilization in the treatment of subacute neck pain, the authors reported an odds ratio of 3.8 (OR=3.8, 95% CI: 0.39-37.18) for patient global impression of change (PGIC) in the Activator group at 12 months compared to baseline, suggestive of a significant probability for a 12-month patient perceived improvement[1]. The authors also reported a statistically and clinically significant improvement for the Activator device from baseline to the 12-month end point in secondary outcome numerical rating scale for pain intensity (NRS) (3.0, 95% CI: 1.93 to 4.69). All groups had pain improvement from baseline to 12 months with no between-group differences. Pain decreased by 3 points in the Activator group, 4 points in the manipulation group, and 3 points in the mobilization group (a reduction in pain of at least 2 points is considered a clinically meaningful improvement). Pain medication or other

treatment for neck pain during the study was not permitted, though a rescue medication was permitted. More patients in the Activator group reported use of the rescue medication compared to mechanical manipulation and mobilization (n=5, 3, and 2, respectively). This reliance on rescue pain medication, along with small sample size, may have influenced the outcomes.

In another study, the instrument-assisted manipulation (IAM) (plus stretching) group was treated with a single cervical manipulation and compared to manually applied manipulation (plus stretching) and to a stretching only control for the treatment of mechanical neck pain[2]. Among the outcomes for pain improvement, there was a reported difference in the change from baseline in outcomes for numerical pain rating scale (NPRS) between IAM (−0.73, 95% CI: -1.40 to −0.05)) and control (0.18, 95% CI: −0.50 to 0.86) at 7 days follow-up, though the difference did not reach statistical significance. There was also a reported difference in the immediate postintervention outcomes for visual analogue score (VAS) between IAM (-1.32, 95% CI:-1.86 to -0.78) and control (-0.50, 95% CI: -1.04 to 0.04) and for pressure pain threshold (PPT) between IAM (0.30, 95% CI: -0.08 to 0.68) and control (-0.23, 95% CI: -0.62 to 0.15), though the differences were not statistically significant There were no between-group differences for IAM compared to MAM or control (only for MAM compared to control) and none of the groups reported changes that were above the minimally clinically important difference for any of the pain outcomes. The use of only a single manipulation and inclusion of patients with low baseline pain may have impacted the outcomes.

The mechanically assisted instrument (MAI) was compared to a placebo (n=65 and 60 patients per group) for treatment of referred shoulder pain in another study[3]. In the MAI group, the frequency of extreme should pain decreased from weekly to monthly ($p<0.05$). Additionally, the proportion of patients who experienced pain on extension/rotation/lateral flexion at 24 weeks compared to preintervention levels decreased by 30% ($p<0.01$) and the proportion of patients experiencing pain in cervical lateral flexion decreased by 20% ($p<0.05$). There were no significant between-group differences for any of the measures of pain, though the treatment group showed improvement over placebo.

In a feasibility sham controlled study for treatment of neck pain in older patients with concomitant non-specific dizziness, the results showed a trend favoring the Activator- assisted group for clinically significant improvement in neck pain[4]. Numeric rating scale (NRS) neck pain scores, presented as the mean (standard deviation (SD)), were found to be clinically significantly reduced pre- to post-intervention [Activator: 4.38 (SD=2.36) to 2.75 (SD=2.49); sham:2.82 (SD=1.78) to 3.60 (SD=2.12)]. Neck Disability Index (NDI) pain scores were also found to be clinically significantly reduced pre- to post-intervention [Activator: 24.94 (SD=12.87) to 19.07 (SD=12.50); sham: 24.18 (SD=8.22) to 22.80 (SD=6.2)]. The authors reported on the proportion of clinically significant improvement (at least 19%) in the primary outcome of NDI; specifically, 58% in the Activator-assisted device group compared to 30% of patients in the sham group.

In another study, a small pilot study (5 patients per group) comparing manual and mechanically assisted manipulation of the thoracic spine in patients with acute or chronic neck pain, the Impulse iQ group was found to be statistically significant in improving VAS pain scores (p=0.015) compared to baseline[5]. There were no significant between-group differences on pain scores (p=0.169). The study showed a wear-off in VAS reduction at 6 months, though this outcome may be influenced by the small sample size. The device group showed no significant improvement in the secondary outcome of neck disability index (NDI) (p=0.061) and there was no significant between-group difference in NDI.

Overall, the studies for treatment of neck pain (including conditions associated with neck pain) provide some evidence of effectiveness, with four of five studies showing some measure of statistical and/or clinical significance on pain outcomes compared to baseline. However, the studies included small and underpowered sample sizes, including two feasibility/pilot studies. Duration and frequency of treatment were variable among studies, ranging from a single treatment to twice per week for six weeks then once per week for three weeks. Use of additional treatment modalities, including exercise and pain medication, was also a variable within and across studies. Follow-up duration was variable, ranging from seven days to 24 months. The level of baseline pain also varied. In one study, low baseline pain and only a single manipulation may have contributed to the lack of clinical significance.

Treatment of Low Back Pain (LBP)

In two studies, one observational and the other an RCT, the plunger-like manipulator was used in the treatment of acute or subacute low back pain compared to manual manipulation[6,7]. In one of the studies, a usual medical care (UMC)[7] control was also used. A total of 88 patients were treated in the plunger-like manipulator device group, and 111 patients in the manual therapy (n=76)[6,7] and UMC control groups combined (n=35)[7]. Follow-up ranged from 3 months to 6 months.

In the observational study, there was a reported significant difference between the unadjusted mean 4-week numeric pain rating scale (NPRS) scores of the two cohorts (mean difference =1.2, p=.011)[6]. There was no significant improvement in Oswestry Disability Index (ODI) score at 4 weeks for the Activator group over baseline. Wide variations in treatment frequency and duration and modalities were found between the cohorts that utilized “treatment as usual” protocols across three centers.

In the RCT, comparison of mechanical-assisted manipulation (MAM) to usual medical care (UMC) showed a non-significant difference for Oswestry LBP disability index (-6.5, 95% CI: −4.4 to 7.5, p=0.609)[7] at 4 weeks. For numeric pain scores, there was also no significant difference between MAM in comparison to UMC (-0.3, 95% CI: −1.2 to 0.6, p=0.480). There was a statistically significant advantage of manual manipulation at 4 weeks compared to MAM (disability = -8.1, p=0.009; pain = -1.4, p=0.002) and UMC (disability =-6.5, p=0.032; pain = -1.7, p<0.001). This study was conducted at a single center designed by a single

investigator; patient-provider interaction possibly could have impacted the outcomes.

The studies for treatment of LBP indicate a lack of effectiveness compared to manual manipulation or usual medical care. The lack of multiple, sufficiently powered studies combined with study limitations, including lack of uniform study conduct and a lack of treatment blinding, preclude clear conclusions.

5.5 Overall Literature Review Conclusions

The literature reports minimal safety risks with three of the seven studies reporting mild and transient adverse events including: increased neck pain, radiating pain, arm weakness, arm numbness, headache, fatigue, dizziness, mid-back pain, stiffness and mild soreness. For the treatment of neck pain, overall, the plunger like joint manipulator was found to be effective, though the studies were small and inadequately powered, thus the data should be interpreted with caution. Four of five studies for treatment of neck pain reported a statistically and/or clinically significant reduction in pain from baseline. For the treatment of low back pain, the plunger-like joint manipulator did not provide statistically and/or clinically significant improvement in pain or disability outcomes compared to manual manipulation or usual medical care.

None of the studies evaluated plunger-like joint manipulators for indications other than spinal manipulation (for treatment of neck pain (or related conditions) or back pain). Though these devices are also cleared for other uses (e.g., extremity manipulation and spinal/extremities mobilization), this literature review did not identify studies for indications other than spinal manipulation in adults.

6. Risks to Health Identified through Medical Device Reports (MDRS)

6.1 Overview of the MDR System

The MDR system provides FDA with information on medical device performance from patients, health care professionals, consumers and mandatory reporters (manufacturers, importers and device user facilities). The FDA receives MDRs of suspected device-associated deaths, serious injuries, and certain malfunctions. The FDA uses MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products. MDRs 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

Although MDRs are a valuable source of information, this passive surveillance system has limitations, including: the submission of incomplete, inaccurate, untimely, unverified, duplicated or biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone due to potential under-reporting of events and lack of information about the frequency of device use. Finally, the existence of an adverse event report does not definitely establish a causal link between the device and the reported event. Because of these limitations, MDRs comprise only one of the FDA's tools for assessing device performance. As such, MDR numbers and data should be taken in the context of the other available scientific information.

6.2 MDR Data: Plunger-Like Joint Manipulators (Product Code LXM)

Individual MDRs for plunger-like joint manipulators are reported through FDA's Manufacturer and User Facility Device Experience (MAUDE) Database, which houses mandatory reports from medical device manufacturers, importers and user facilities, as well as voluntary reports from entities such as health care professionals, patients and consumers.

The Agency searched the Medical Device Report (MDR) database on March 9, 2021 to identify adverse events related to the use of Plunger-Like Joint Manipulator devices (Product Code LXM) entered between April 1, 1988 and December 31, 2020. The search identified 5 relevant MDRs.

The 5 reported adverse events were entered into the System for Uniform Surveillance (SUS) database between March 12, 2009 and February 2, 2018 and included Injury (N= 4) and Malfunction (N= 1) reports. The majority of the reports originated from the United States (N= 4) and one report originated from an unknown reporting country. Patient age was reported in 3 MDRs and ranged from 32 years to 50 years of age:

- The Injury MDRs (N= 4) were voluntary reports that note an unspecified injury (N=2), pain and hearing loss (N= 1), and pain, paralysis, and dyspnea (N=1). Three reports of injury noted issues with general use of the device and one MDR noted issue with the design and quality of the device.

- The Malfunction MDR (N=1) was a manufacturer report that noted failed repair of the device and no known patient involvement.

7. Recall History

7.1 Overview of Recall Database

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 may occur after the firm recalling the medical device product conducts and communicates with its customers about the recall. Therefore, the recall information posting date ("create date") identified on the database indicates the date FDA classified the recall, it does not necessarily mean that the recall is new.

7.2 Recall Results: Plunger-Like Joint Manipulators

One Class II recall[1] has been identified in the Medical Recall Database with the product code LXM. A Model 8000 Atlas C-1 Orthogonal Adjusting Instrument was recalled in 2013 because the firm was marketing their device without marketing authorization.

8. Summary

In light of the information available, the Panel will be asked to comment on whether plunger-like joint manipulators under product code “LXM”:

meet the statutory definition of a Class III device:

- insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of its safety and effectiveness, 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

or would be more appropriately regulated as Class II, in which:

- general and special controls, which may include performance standards, postmarket surveillance, patient registries and/or development of guidelines, are sufficient to provide reasonable assurance of safety and effectiveness

or as Class I, in which:

- the device is subject only to general controls, which include registration and listing, good manufacturing practices (GMPs), prohibition against adulteration and misbranding, and labeling devices according to FDA regulations.

For the purposes of classification, FDA considers the following items, among other relevant factors, as outlined in 21 CFR 860.7(b):

1. The persons for whose use the device is represented or intended;

[1] Recalls are classified into a numerical designation (I, II, or III) by the FDA to indicate the relative degree of health hazard presented by the product being recalled. A Class II recall is a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

2. The conditions of use for the device, including conditions of use prescribed, recommended, or suggested in the labeling or advertising of the device, and other intended conditions of use;
3. The probable benefit to health from the use of the device weighed against any probable injury or illness from such use; and
4. The reliability of the device.

8.1 Special Controls

FDA believes that special controls, in addition to general controls, can be established to mitigate the risks to health identified, and provide a reasonable assurance of the safety and effectiveness of plunger-like joint manipulators. Following is a risk/mitigation table, which outlines the identified risks to health for this device type and the recommended controls to mitigate the identified risks:

Table 3: Summary of Risks to Health and Proposed Special Controls for Plunger-Like Joint Manipulators

Identified Risk	Recommended Mitigation Measure
Adverse tissue reaction	• Biocompatibility evaluation
Electric shock or burn	• Electromagnetic compatibility (EMC) testing • Electrical, mechanical, and thermal safety testing
Pain	• Electromagnetic compatibility (EMC) testing • Electrical, mechanical, and thermal safety testing • Non-clinical performance testing • Software verification, validation, and hazard analysis • Labeling
Discomfort	• Electromagnetic compatibility (EMC) testing • Electrical, mechanical, and thermal safety testing • Non-clinical performance testing • Software verification, validation, and hazard analysis • Labeling
Tissue injury	• Electromagnetic compatibility (EMC) testing • Electrical, mechanical, and thermal safety testing • Non-clinical performance testing • Software verification, validation, and hazard analysis • Labeling

The Panel will be asked whether this list is a complete and accurate list of the risks to health presented for plunger-like joint manipulators and whether any other risks should be included in the overall risk assessment of the device type.

Based on the identified risks and recommended mitigation measures, FDA believes that the following special controls would provide reasonable assurance of safety and effectiveness for plunger-like joint manipulators under product code "LXM":

1. The patient contacting components of the device must be demonstrated to be biocompatible.

2. Electromagnetic compatibility and electrical, mechanical, and thermal safety testing must be performed.

3. Non-clinical performance testing must characterize the thrust force applied to the patient.

4. Software verification, validation, and hazard analysis must be performed.

5. Labeling must include:

    (i) A warning that the device could cause pain, including neck pain, radiating pain, mid-back pain and tissue injury.
    (ii) A warning that the device could cause discomfort, including headache, fatigue, dizziness, stiffness, mild soreness, arm weakness, and arm numbness.

If the Panel believes that Class II is appropriate for plunger-like joint manipulators under product code "LXM," the Panel will be asked whether the identified special controls appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

8.2 Overview of Proposed Classification/FDA Recommendation

Based on the safety and effectiveness information gathered by the FDA, the identified risks to health and recommended mitigation measures, we recommend that plunger-like joint manipulators indicated for use to perform chiropractic adjustment or manipulation be regulated as Class II devices.

882.5055. Plunger-like joint manipulator.

(a) *Identification.* A plunger-like joint manipulator is an electromechanical device intended to perform chiropractic adjustment or manipulation of the spinal column and/or extremities. Joint manipulation is achieved through a thrust force delivered to the patient via a plunger attached to a metal stylus, positioned over the desired region of the vertebra.

(b) *Classification.*

Class II (special controls). The special controls for this device are:

1. The patient contacting components of the device must be demonstrated to be biocompatible.

2. Electromagnetic compatibility and electrical, mechanical, and thermal safety testing must be performed.

3. Non-clinical performance testing must characterize the thrust force applied to the patient.

4. Software verification, validation, and hazard analysis must be performed.

5. Labeling must include:

    (iii) A warning that the device could cause pain, including neck pain, radiating pain, mid-back pain and tissue injury.
    (iv) A warning that the device could cause discomfort, including headache, fatigue, dizziness, stiffness, mild soreness, arm weakness, and arm numbness.

Based on the available scientific evidence, the FDA will ask the Panel for their recommendation on the appropriate classification of plunger-like joint manipulators under product code "LXM."

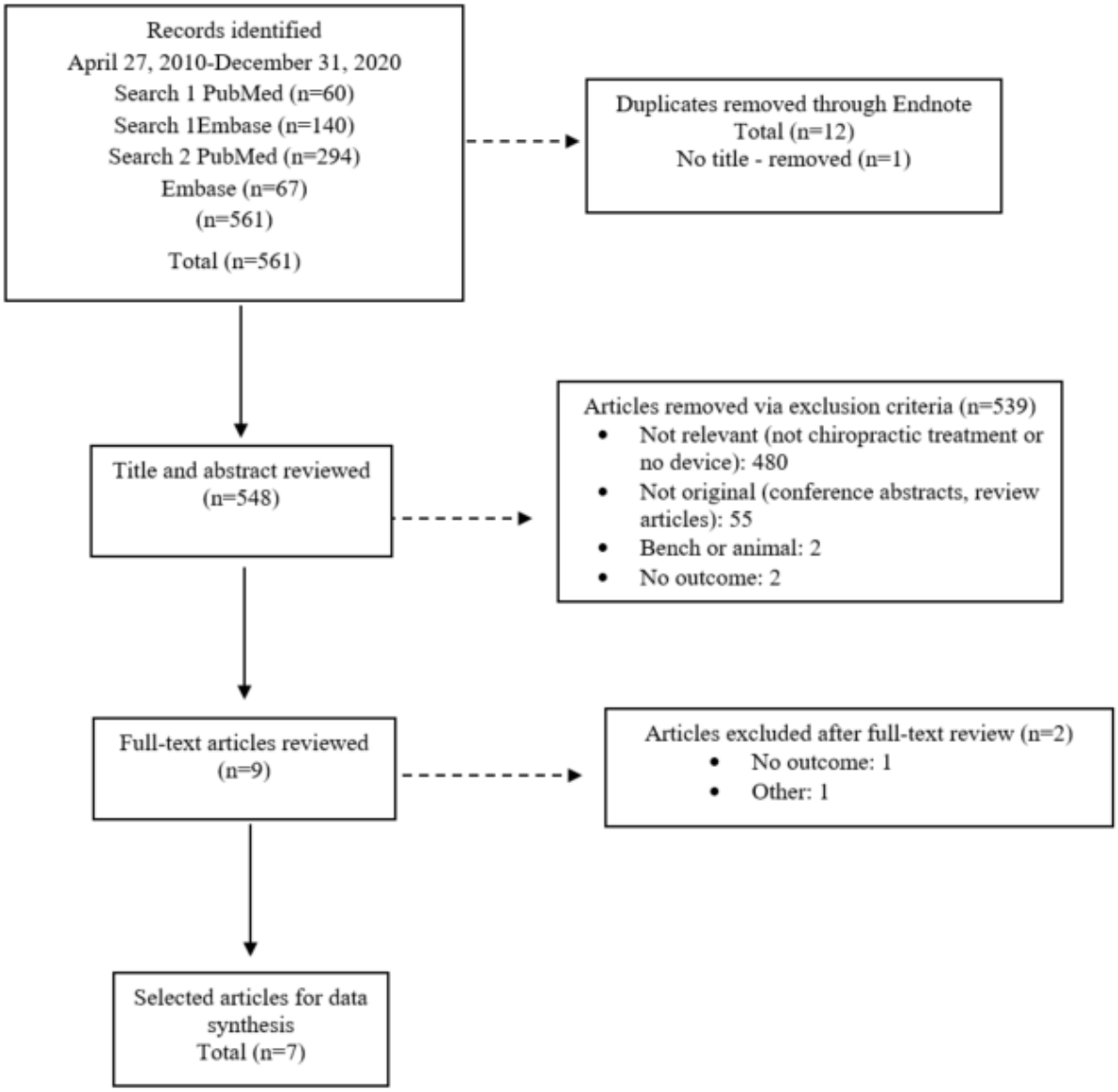
Appendix A: Literature Search Terms and Filters for Plunger-like Joint Manipulators

Online literature searches were performed in two electronic databases (PubMed and Embase), with two sets of search terms used in sequence. The first search (1) was performed with the search terms identified below. After cross-checking the articles for all relevant studies, additional articles were found with the trade name “Activator.” Accordingly, an additional search (2) was performed using the trade name Activator and same pre-defined search limits. The search was limited to human studies and published in English language, with publication dates between April 27, 2010 and December 31, 2020.

1. ((mechanically assisted manipulation) OR (assisted manipulation) OR (hand held chiropractic instrument) OR (torque instrument)) AND (spine OR spinal OR vertebral OR extremities) AND ((neck pain) OR (low back pain) OR (recurrent pain) OR (vertebral adjustment) OR (vertebral alignment) OR (Atlas adjustment) OR (cervical adjustment) OR (spinal mobilization) OR (musculoskeletal joint manipulation) OR (spinal subluxation) OR (back strain) OR (cervicalgia) OR (low back strain) OR (lumbargo))

2. (Activator spinal manipulation)

Appendix B: Flow Diagram of Systematic Literature Review Search Results



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Classification of Plunger-Like Joint Manipulators
FDA Questions

Neurological Devices Panel of the Medical Devices Advisory Committee June 3-4, 2021

1. FDA has identified the following risks to health for plunger-like joint manipulators:

Identified Risk	**Description/Examples**
Adverse tissue reaction	This can result from use of device materials that are not biocompatible.
Electric shock or burn	This can result from electrical failure or malfunction.
Pain	This risk could be due to a mechanical, electrical or software malfunction causing device failure. Types of pain include neck pain, radiating pain, and mid-back pain.
Discomfort	This risk can be caused by a mechanical, electrical, or software malfunction causing device failure. Types of discomfort include headache, fatigue, dizziness, stiffness, mild soreness, arm weakness, and arm numbness.
Tissue Injury	This risk could be due to a mechanical, electrical or software malfunction causing device failure. An example of tissue injury includes bruising from excessive force or pressure.

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of plunger-like joint manipulators under product code "LXM". In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these plunger-like joint manipulators.

2. 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

    - if, in addition, 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.

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
    I. 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
    II. does not present a potential unreasonable risk of illness or injury.

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 plunger-like joint manipulators. Following is a risk/mitigation table which outlines the identified risks to health for this device type and the recommended controls to mitigate the identified risks.

Risk/mitigation recommendations for plunger-like joint manipulators under product code "LXM"

Identified Risk	**Recommended Mitigation Measure**
Adverse tissue reaction	• Biocompatibility evaluation
Electric shock or burn	• Electromagnetic compatibility (EMC) testing • Electrical, mechanical, and thermal safety testing
Pain	• Electromagnetic compatibility (EMC) testing • Electrical, mechanical, and thermal safety testing • Non-clinical performance testing • Software verification, validation, and hazard analysis • Labeling
Discomfort	• Electromagnetic compatibility (EMC) testing • Electrical, mechanical, and thermal safety testing • Non-clinical performance testing • Software verification, validation, and hazard analysis • Labeling

Identified Risk	Recommended Mitigation Measure
Tissue injury	• Electromagnetic compatibility (EMC) testing • Electrical, mechanical, and thermal safety testing • Non-clinical performance testing • Software verification, validation, and hazard analysis • Labeling

Please discuss whether the identified special controls for plunger-like joint manipulators appropriately mitigate the identified risks to health and whether additional or different special controls are recommended:

1. The patient contacting components of the device must be demonstrated to be biocompatible.

2. Electromagnetic compatibility and electrical, mechanical, and thermal safety testing must be performed.

3. Non-clinical performance testing must characterize the thrust force applied to the patient.

4. Software verification, validation, and hazard analysis must be performed.

5. Labeling must include:

   (i) A warning that the device could cause pain, including neck pain, radiating pain, mid-back pain and tissue injury.
   (ii) A warning that the device could cause discomfort, including headache, fatigue, dizziness, stiffness, mild soreness, arm weakness, and arm numbness.

3. **Please discuss whether you agree with FDA's proposed classification of Class II with special controls for plunger-like joint manipulators devices. If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.**