FDA Executive Summary

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

Classification of Electro-Acupuncture Stimulators

Product Code: BWK

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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 electro-acupuncture stimulators, a pre-amendments device type which remains unclassified. Specifically, the FDA will ask the Panel to provide recommendations regarding the regulatory classification of electro-acupuncture stimulators under product code "BWK". 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 "BWK" remain unclassified.

FDA is holding this Panel meeting to obtain input on the risks to health and benefits of electro-acupuncture stimulators under product code "BWK." The Panel will discuss whether electro-acupuncture stimulators under product code "BWK" should be classified into class II (subject to General and Special Controls).

1.1 Current Regulatory Pathways

Electro-acupuncture stimulators are a pre-amendments 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

An electro-acupuncture stimulator is designed to function based on a principle of traditional Chinese medicine, that stimulation of certain areas of the body (acupuncture points) can have a physiological influence on non-adjacent body parts or organ systems. The device applies a low voltage electric current to stimulate these acupuncture points via percutaneous or transcutaneous electrodes. Some devices also measure skin conductance to identify acupuncture points by their high conductivity or come with accessory applicators intended to aid in placement of acupuncture needles.

Almost all cleared devices apply the electric current across two electrodes on the skin. Devices can be used with separate 510(k)-cleared acupuncture needles or needl electrodes supplied with the device. At least one cleared device, the Selectrode System, employs a belt or garment with holes corresponding to acupuncture points on the wearer through which an electrically conductive liquid is applied to cutaneous electrodes. Another device, the ACULIFE, applies electrical stimulation to acupuncture points in the hand via one probe electrode and one cutaneous electrode.

2. Regulatory History

The Health Point device manufactured by Anritsu America Co. was the first device under product code BWK to be cleared by FDA on April 3, 1979. The FDA determined that the Health Point device was substantially equivalent to Chan's Locator Stimulator LTA-3S, a pre-amendments device. Since this 510(k) clearance, 19 devices have been cleared under the unclassified product code BWK (see Table 1).

Table 1: 510(k) clearances for electro-acupuncture stimulators under product code "BWK"

510(k) Number	Trade Name	Sponsor
K781651	Health Point	Anritsu America Co.
K832634	Selectrode System	Bio-Stimu Trend Corp.
K840983	Pulselife Stimulator	Pulse Life Inc.
K840995	Acupuncture Insoles	Lu lu Enterprise Co. Ltd.
K014273	Acustim	S.H.P. Intl. Pty. Ltd.
K050123	P-Stim System	Neuroscience Therapy Corp.
K051197	Aculife Model Smw-01	Inno-Health Technology Inc.
K081943	Model ES-130	Ito Co. Ltd.
K091875	E-Pulse	Medevice Corporation
K091933	Electro-Acupuncture: Aculife/Model IDOC-01	Inno-Health Technology Inc.
K093322	Multi-Purpose Health Device	UPC Medical Supplies Inc. DBA United Pacific Co.
K122812	Jiajian Electro-Acupuncture Stimulators	Wuxi Jiajian Medical Instrument Co. Ltd.
K130768	Jiajian CMN Stimulator	Wuxi Jiajian Medical Instrument Co. Ltd.
K133980	Pantheon Electrostimulator	Pantheon Research
K140530	Electro Auricular Device	Navigant Consulting Inc.
K140788	P-Stim	Biegler Gmbh
K141168	Ansistim	Dyansys Inc.
K152571	Stivax	Biegler GMBH
K170391	Ansistim-PP	Dyansys Inc

3. Indications for Use

The Indications for Use (IFU) statement identifies the condition and patient population for which a device should appropriately be used. Many indications for electro-acupuncture stimulators are generally for use in the practice of acupuncture. Some IFU statements specify one or both of the two components of acupuncture practice: the identification of

acupuncture points, and the stimulation of acupuncture points. A subset of devices is designated only for acupuncture points on the auricle, while another subset is designated only for acupuncture points on the hands. All devices are indicated for prescription use.

Based on the IFUs and labeling cleared in the 510(k)s noted in Table 1, representative indications for use for electro-acupuncture stimulators under product code "BWK" include:

- To be used in the practice of acupuncture
- For pain relief
- Treatment of chronic pain
- Does not have curative value but stimulates appropriate auricular acupuncture points
- Acute Pain: Post–operative pain
- Chronic Pain: Chronic back pain, Cervical syndrome, migraine
- Pain associated with joint disease or primary and secondary neuralgias.

4. Clinical Background

4.1 Disease Characteristics

Pain is an unpleasant feeling that is associated with both a physical response to nociception, and an emotional component which may be influenced by real or perceived potential for future nociception or injury. Pain describes the subjective sensation of discomfort caused by either actual or potential injury to the body and it can be described in terms of location, intensity, duration, and nature. Pain and the discomfort it causes are subjectively interpreted by individual patients, which may ultimately affect physical, social and emotional function to different degrees. Chronic pain is defined as pain which lasts longer than three to six months, or beyond the duration required for normal tissue healing after an acutely painful event. Pain can be classified as nociceptive, neuropathic, and/or centralized, and the distinction between types of pain influence the treatment plan. The physiology of pain is complex but can be generally described as painful stimuli arising in the periphery, which are subsequently received by nociceptors which communicate peripheral nociceptive input to the dorsal horn of the spinal column where interneuron modulation occurs as the signals are distributed to other structures of the CNS including the brainstem, limbic system, and somatosensory regions of the cortex. The transmission of pain and modulation of the signaling, involve multiple widely distributed bidirectional pathways of excitatory and inhibitory receptors and neurotransmitters serving as targets for pain treatments in the form of drugs and physical interventions.

4.2 Patient Outcomes

Patients with chronic pain require ongoing evaluation, education, and reassurance, as well as help in setting reasonable expectations for response. Current chronic pain

treatments often result in improvement but not elimination of pain (30 percent reduction on average is typical). However, even a 30 percent pain reduction can be meaningful to the patient. Central sensitization of pain can occur as a consequence of persistent noxious stimulation of either nociceptive or neuropathic causes. Central sensitization causes persistent, and often hypersensitivity to pain despite limited input from the peripheral nervous system. The effects of pain on physical function, emotional health, social function and quality of life, are far reaching. The treatments for pain must be chosen with care to prevent worsening function at the expense of improvement in the patient's subjective pain report.

4.3 Currently Available Treatment

Treatment and management of pain is complex and continues to evolve. The appropriate therapeutic strategy for the treatment of pain is dependent upon accurate evaluation of the cause of pain, as well as the type and chronicity of the pain condition. Whenever possible, a nociceptive or neuropathic source for the underlying cause of pain should be identified and targeted for treatment. Examples of targeted disease-specific treatments include correction of structural deformities causing nociceptive pain, decompression of peripheral nerves causing neuropathic pain, and use of disease-modifying antirheumatic treatments which may reduce or possibly eliminate the need for analgesic drugs.

Chronic pain is best managed with collaborative multidisciplinary support including primary care, psychology or other behavioral health specialists, physical therapy, use of appropriate physical modalities including interventional pain, and complementary and alternative health therapies. Involving patients in their care through education on the mechanisms that contribute to chronic pain can reduce fear and anxiety which hinder improvement. It is important for the team to set reasonable expectations for response in order to achieve successful chronic pain management.

Nonpharmacologic therapies for chronic pain include:

- Exercise therapy
- Cognitive behavioral therapy
- Patient education
- Mind-body therapies (Mindfulness-based stress reduction)
- Physical interventions:
    - Physical modalities: (transcutaneous nerve stimulation (TENS), heat, ultrasound etc.)
    - Chiropractic manipulation
    - Massage
    - Acupuncture
    - Trigger point injections and dry needling

Pharmacologic therapy can be considered for patients with inadequate analgesia despite nonpharmacologic therapies. The optimal choice of pharmacologic therapy

depends on the type of chronic pain syndrome, and neuropathic pain should be distinguished from nociceptive pain since treatments differ. The patient's medical status (e.g., cardiovascular, hepatic, renal, and cognitive issues) may affect the choice of drug, due to potential for drug side-effects, drug clearance, and drug-drug interactions. Medications include: NSAIDS, acetaminophen, antidepressants, and anti-epileptic drugs. Finally, opioids can be considered when the benefits outweigh the potential risks and when other therapies have failed to provide adequate pain relieve and improvement in function. While opioids can be highly effective for acute pain, the role of opioids for chronic nociceptive pain is uncertain. Based on evidence of risk and absent strong evidence of effectiveness, long-term opioids should not routinely be used for chronic pain. If opioids are necessary, they should be used at the lowest effective dose, with ongoing reassessment of risks and benefits.

Interventional therapy for chronic pain ranges from office-based injections into muscles or joints, to neuro-destructive or neuromodulatory procedures used to treat more widespread pain. Interventional therapy typically attempts to target the presumed pain generators and can be used in conjunction with rehabilitation and appropriate pharmacotherapy.

Sleep disturbances are common consequences of chronic pain and patients with insomnia or disrupted sleep should be treated with evidence-based nonpharmacologic measures including improved sleep hygiene, stimulus control and cognitive behavioral therapy. For patients who require pharmacotherapy, melatonin, or if necessary and appropriate, more sedating tricyclics for both antidepressant and analgesic benefits, can be tried.

4.4 Risks

FDA has identified the following risks to health associated with electro-acupuncture stimulators:

Table 2: Risks to Health and Descriptions/Examples for Electro-acupuncture stimulators

Identified Risk	Description/Examples
Adverse tissue reaction	• Skin irritation • Local pain • Changes in skin pigmentation such as hematoma and skin pallor
Infection	• Infection due to non-sterile/contaminated needle and other types electrodes that enters epidermis or deeper layer of the skin • Sepsis

Identified Risk	Description/Examples
Patient injury or discomfort, including: • electrical shock or burn • bleeding	• Excessive trauma, perforation of blood vessels and organs caused by needles leading to bleeding, ecchymosis, hematoma • Electrical shock or burn • Muscle cramping
Use error	• User discomfort, tissue injury, or delayed treatment

The Panel will be asked whether this list is a complete and accurate list of the risks to health presented by electro-acupuncture stimulators under product code "BWK" 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 was conducted in an effort to gather any published information regarding the safety and effectiveness of electro-acupuncture stimulators under product code "BWK."

We searched two electronic databases, PubMed and Embase, for journal articles published from January 1, 2010 to December 31, 2020. The search was limited to human clinical studies with full text available in English language with focus on the following indications: pain, neurological and muscular conditions, and vomiting/nausea (search terms detailed in **Appendix A**). Multiple searches were conducted using product names combined with brand names and related terminologies without the limitation of indication of use. Additionally, for device effectiveness, references were further limited to randomized clinical trials (RCTs), meta-analyses using RCTs, and systematic literature reviews (SLRs) using RCTs (i.e., highest-level of evidence) due to the large number of studies that evaluated electro-acupuncture (EA) effectiveness; all published studies, including case reports, were extracted for device safety. Detailed methods, search terms and filters are provided in **Appendix A**.

5.2 Results

The search yielded 2,953 initial literature references. After duplicate articles were removed between databases, a total of 2,582 articles remained. Following a review of the titles and abstracts, a total of 570 articles remained for full-text review. Of these, 105 articles were determined to be relevant to the safety and effectiveness of electro-acupuncture stimulators. The number of each excluded criterium is also summarized in the flow diagram in **Appendix B**. The 105 selected studies consisted of 73 randomized clinical trials, 13 meta-analyses, seven systematic literature reviews, seven prospective studies, and five case series/reports. Of the selected studies, 95 were conducted outside

of the United States (OUS), eight in the United States, and two both in the US and OUS. 10 of the 105 selected studies report on device safety only, 77 report only device effectiveness, and 18 report both device safety and effectiveness.

5.3 Adverse Events Associated with Electro-Acupuncture Stimulators

Reported adverse events were sporadic across selected indications. Out of the 28 full-text articles reviewed for device safety, 17 reported adverse events (AE) for electro-acupuncture stimulators use in the selected indications.[1-28] Eleven of the studies, including 4 RCTs, 5 prospective cohorts, 1 retrospective cohort, and 1 case series, reported no AEs or electro-acupuncture related events.

The 17 studies reporting AEs related to electro-acupuncture (EA) stimulation were comprised of 3 meta-analyses, 3 SLRs, 8 RCTs and 3 case reports. The types of EA stimulation-related AEs reported are mild fainting, ecchymosis, mild hematoma, nausea, skin pallor, skin pigmentation, vertigo, chest tightness, vomiting, unconsciousness, and death. The counts for specific AEs were provided in two publications. EA stimulation-related AEs reported in SLR of case series included death (n=3), unconsciousness (n=5), chest tightness (n=6), vertigo (n=7), vomiting (n=6), pallor (n=8), and skin pigmentation (n=8). The three deaths were related to internal organ injury involving schizophrenic patients (two deaths from spinal cord injuries at a cervical level and one from cardiovascular injury). However, this case series is the only instance of this type of injury; further detail of case selection and adequate human protection was not found.[8] A meta-analysis of post-operative nausea and vomiting and knee osteoarthritis respectively reported one AE of mild fainting each.[20,29] Another meta-analysis and SLR of RCT's reported electroacupuncture site ecchymosis and no other AEs for musculoskeletal pain.[21,22] In another meta-analysis and separate SLR, no serious AEs and only mild AEs such as mild hematoma and nausea were reported respectively.[23,24]

Among the three RCTs comparing treatment groups, one RCT comparing EA stimulation treatment against conventional treatment in patients with acute ischemic cerebral palsy reported 2.94% (5/170) of the EA stimulation patients with distending pain.[12] Another RCT compared EA stimulation treatment to manual acupuncture in patients with plantar heel syndrome and noted no difference in sharp pain reported in both groups.[9] An RCT comparing EA stimulation treatment against manual acupuncture in patients with knee osteoarthritic pain noted that AEs were uncommon and statistically nonsignificant between treatment groups.[13]

Among the five RCT's reporting AEs with no comparison between groups, the AEs reported were localized bruising, localized skin irritation, mild exacerbation of chemotherapy-induced nausea and vomiting (CINV), neck pain, bruises, pain at acupoints, chest discomfort, itching palm, and warm feeling in the back. A study examining nausea and vomiting in patients having first cycles of moderately or highly emetogenic chemotherapy between EA stimulation, sham EA stimulation, and control group reported mild exacerbation of CINV (n=12), localized bruising (n=5), and

localized skin irritation (n=3).[5] Another study reported mild pain or bleeding after electroacupuncture treatment in patients with ischemic stroke undergoing elective carotid artery stenting with local anesthesia, but no serious AEs were reported.[7] Other studies reported AEs for musculoskeletal pain such as neck pain, bruises, pain at acupoint, chest discomfort, itching palm and warm feeling in the back with statistically nonsignificant differences between EA stimulation treatment groups and sham EA stimulation groups.[15,24,30]

Among the four non-RCT studies that report AEs, only three separate case reports detailed specific AEs from a patient's treatment. The AEs included minor tissue damage due to high intensity EA stimulation treatment from a non-charge-balanced waveform[31] and three cases of skin pigmentation where the anode needle was inserted and four additional cases of skin pigmentation where the anode needle was inserted.[25,32]

The most serious reported AE event is death. Three deaths were reported among patients treated for schizophrenia, but these may be the result of insufficient patient protections. The three most frequently reported AE's were mild exacerbation of CINV, skin pallor and skin pigmentation. Most articles did not include counts of AEs, so it is difficult to discern the true most frequent AE's. There does not seem to be a statistical difference between EA stimulation and manual acupuncture in regard to AE incidence based on the 3 RCT's comparing AE rates between treatment types. Due to the paucity of data for EA stimulator AE frequency as well as difficulties in determining whether an AE is truly related to EA stimulation, more evidence is needed to determine whether the usage of EA is consistently associated with the AE events reported.

5.4 Effectiveness Associated with Electro-Acupuncture Stimulators

Out of the 95 full-text articles reviewed for device effectiveness, 42 reported for musculoskeletal pain, 17 for post-operative pain and analgesic reduction, 6 for neuropathic pain, 4 for stroke, 5 for stroke rehabilitation, 1 for cerebral palsy, 3 for Parkinson's disease, 1 for cerebral infarction, 2 for carpal tunnel syndrome, 4 for fatigue, 2 for headache/migraine, 6 for post-operative nausea/vomiting, 1 for fibromyalgia, and 1 for motion sickness. No studies were found with the inclusion criteria for the indication of visceral pain, Bell's Palsy, chronic fatigue or fibromyalgia. Results are presented by indications below.

5.4.1 Pain

Musculoskeletal Pain

Of the selected studies, 42 studies report on EA stimulation effectiveness in treating musculoskeletal pain.[4,9,13,15,16,19,21,22,27,29,30,33-62] Of these 42 studies, 7 are meta-analyses composed of only RCTs, 4 studies are SLRs and 31 are RCTs. The literature demonstrates that EA stimulation treatment seems to have a significant effect on musculoskeletal pain control compared to sham and control groups (conventional treatment or no treatment) but does not seem to have a significant effect compared to manual acupuncture or alternative treatments.

Of the seven meta-analyses, five showed that EA stimulation treatment of musculoskeletal pain was effective compared to pharmacological treatment, manual acupuncture, sham treatments, conventional care and no intervention. Two meta-analyses showed no statistically significant effect between medical treatment/active comparator and EA stimulation treatment. Of the meta-analyses that showed significant effect of EA stimulation, one meta-analysis yielded different conclusions in that EA stimulation showed a statistically significantly better effect compared to other medications such as pharmacological treatment (RR=1.14; 95% CI=1.01~1.28; P=0.03; heterogeneity: I^2= 0%, P=0.72) and manual acupuncture (RR=1.12; 95% CI=1.02~1.22; P=0.02; heterogeneity: I^2= 0%, P=0.58). The authors also concluded that EA stimulation treatment groups experienced a statistically greater reduction in pain intensity than those who received other medications (standard mean difference in visual analog scale (VAS)=-1.11, 95% CI=1.33~0.88; P < 0.001; heterogeneity: I^2= 41%, P=0.11). EA stimulation was found to be statistically significant (P<0.05) in relieving pain and improving function in knee osteoarthritis patients over sham needle control groups (VAS mean difference (MD)= -1.16, 95% CI=-1.51~-0.82]; MD = -3.34, 95% CI=-4.68~-1.99). Additionally, acupuncture, EA stimulation, and warm needle were better than education and no intervention control (VAS MD = - 2.09, 95%CI =-2.15~-2.03; MD = -6.60, 95%CI=-6.97~-6.22]).[29]

Another meta-analysis corroborated these findings by demonstrating that EA stimulation could relieve pain in patients with osteoporosis (MD=–1.32, 95% CI=–2.15~–0.48, P=0.002).[22] Two more meta-analyses showed that EA stimulation treatment statistically significantly reduced pain in patients with knee osteoarthritis and mechanical neck disorders compared to conventional care (P<0.05).[52,53] Conversely, a Bayesian meta-analysis of 13 RCTs found no statistical significance in pain control between the EA stimulation treatment group and a medical treatment group (using a random-effect model) using direct meta-analysis. In addition, the authors found no statistically significant effect between EA stimulation and transcutaneous electrical nerve stimulation (TENS) using network meta-analysis.[63,64]

Out of four SLRs, two publications reported that EA stimulation treatment statistically significantly reduced VAS compared to TENS treatment for patients with myofascial pain and stroke (P<0.05).[50,65] Another two SLRs reported that EA stimulation was more effective than placebo treatment or conventional treatment in patients with musculoskeletal disorders and carpal tunnel syndrome respectively.[21,54]

Among 31 RCTs reporting on EA stimulation for musculoskeletal pain, ten RCT results were statistically significant (P<0.05) in that EA stimulation reduced VAS or numerical rating pain scale (NRPS) compared to control groups, but 22 RCTs reported that EA stimulation pain control was statistically nonsignificant compared

to sham EA stimulation groups or manual acupuncture.[4,9,13,15,19,30,36-40,44,46-48,55,56,66-68]

Post-Operative Pain and Post-Operative Analgesic Use

Of the selected studies, 17 were RCT that examined EA stimulation effectiveness in treating post-operative pain.[2,7,11,67-80] Select RCTs showed that EA stimulation had a statistically significant effect on pain reduction compared to sham EA stimulation and control, but these studies did not have comparisons to manual acupuncture ($P<0.05$).[60,70,71,78,80] In one RCT of outpatients who underwent selective colonoscopy, there were fewer occurrences of post-procedural abdominal pain (11.4% vs 25.2%, $P = 0.007$) and distension (1.8% vs 7.8%, $P = 0.032$).[67] Another RCT showed that at 1 hour, the EA stimulation treatment group showed statistically significant higher reduction in VAS score compared to control ($P=0.013$) and sham EA stimulation groups ($P=0.009$).[73] Some RCT reports noted that there was a statistically significant pain reduction effect acutely but pain reduction became statistically nonsignificant compared to other treatments after 24 hours.[11,68,74-77] However, another RCT showed that when using the MacGill Pain Questionnaire along with VAS scores, there was no statistically significant difference in pain relief after 48 hours compared to manual acupuncture.[28]

For analgesic reduction, three RCT reports noted that EA stimulation had a significant effect in reducing post-operative analgesic use. For one RCT, mean cumulative opioid usage was statistically lower in the EA stimulation group at 1 to 4 hours post-surgery compared to the control group ($P<0.05$).[69] Another RCT demonstrated that there was a 20% reduction in analgesic use for the EA stimulation treatment group versus the sham EA stimulation treatment group.[70] The third RCT also showed that EA stimulation at acupoints had statistically significant longer time to first demand for analgesia for an EA stimulation treatment group (92.0 ± 82.7 min) compared to control groups (34.1 ± 22.0 min) ($P<0.001$).[79]

Neuropathic Pain

Of the selected studies, six reported on EA stimulation effectiveness in treating neuropathic pain: two meta-analyses, three RCTs and one case series.[10,81-85] One meta-analysis of 13 RCTs reported that EA stimulation treatment was superior to control treatment in patients with migraine. Network meta-analysis further reported that there were statistically different VAS scores for EA stimulation compared to sham EA stimulation, acupuncture with sham-EA stimulation, acupoint catgut embedding with sham EA stimulation, and acupoint catgut embedding with blank controls ($P<0.01$).[83] Another meta-analysis corroborated these findings, noting a statistically significantly improved VAS and NRPS in the EA stimulation treatment group compared to a control group in patients with reflex sympathetic dystrophy after stroke ($P<0.05$).[84] One RCT reported that EA stimulation treatment had no statistically significant difference in neuropathic pain management compared to a placebo-EA treatment for patients with chronic peripheral neuropathy.[82] Another

RCT demonstrated that in patients with post-herpetic neuralgia irritable nociceptor type, the EA stimulation treatment group plus conventional treatment had a statistically significant reduced average daily pain score (ADPS) compared to the sham-EA stimulation plus conventional treatment group (P<0.001).[81] A case series of 12 patients with chronic neuropathic pain used StimScore to measure pain and demonstrated that 58% (7/12) were treated successfully and in 42% (5/12) treatment was unsuccessful.[10]

5.4.2 Neurological and Muscular Conditions

Stroke

For the stroke indication, four studies, including one meta-analysis and three RCTs, reported effectiveness outcomes for EA stimulation treatment.[7,18,86,87] The meta-analysis reported that amongst 18 RCTs looking at acute ischemic stroke, EA stimulation treatment improved Barthel Index scores (SMD 0.72, 95% CI=0.35~1.08, P<0.001), Fugel-Meyer Assessment (SMD 0.98, 95% CI=0.75-1.22, P<0.001), National Institutes of Health Stroke Scale (NIHSS) (SMD -0.81, 95% CI=-1.14~-0.49, P<0.001) and Revised Scandinavian Stroke scale (SMD -1.27, 95% CI=-2.18~-0.37, P<0.00001) compared to western traditional treatments. This meta-analysis demonstrated a statistically significant difference in clinical effectiveness between EA stimulation and western traditional treatments (P<0.001).[87] One RCT corroborated those findings in patients with acute ischemic stroke for both the NIHSS and the Barthel Index (P<0.05).[18] The results of another RCT indicated that EA stimulation treatment groups had statistically significant improvements in NIHSS and GES scores compared to sham EA stimulation groups[7] and an additional RCT noted a statistically significant improvement for EA stimulation treatments in NIHSS score compared to a control group (P<0.05).[86]

Stroke Rehabilitation

For stroke rehabilitation, two meta-analyses and three RCTs reported on EA stimulation effectiveness outcomes.[84,87-90] One meta-analysis demonstrated that EA stimulation treatment was statistically significant in improving the Barthel Index compared to controls in patients with reflex sympathetic dystrophy after stroke (WMD = 12.170, 95% CI=6.657~17.682, P<0.001).[84] The other meta-analysis showed that EA stimulation with conventional western treatment improved the NIHSS (SMD -0.81, 95% CI=-1.14~-0.49, P<0.001) and Chinese Stroke Recovery scale (SMD -1.27, 95% CI=-2.18~-0.37, P<0.001) compared to conventional treatment alone.[87] While one RCT demonstrated that EA stimulation treatment was effective and that language brain areas in patients with motor aphasia post-stroke were activated by EA stimulation treatment, another showed statistically nonsignificant improvement in regard to elbow and wrist joint spasticity for EA stimulation treatment groups compared to controls after 6 weeks.[90] One more RCT noted NIHSS improvement with EA stimulation treatment, but statistically nonsignificant changes when compared to control.[89] EA stimulation treatment

seems to have varied effects in regard to stroke rehabilitation and further studies are needed before concrete conclusions can be drawn.

Cerebral Palsy

A single RCT evaluated EA stimulation for treatment of spastic cerebral palsy and concluded that EA stimulation was more effective than manual acupuncture in reducing the root mean square of the gastrocnemius muscle tone and modified Tardieu Scale in children with spastic cerebral palsy. Additional studies are needed to assess the effectiveness of these devices for cerebral palsy.[91]

Parkinson's Disease

An RCT indicated that in patients with Parkinson's disease, EA stimulation treatment resulted in statistically significant effects in gait functionality compared to sham EA stimulation treatment for single task habitual walking, single task fast walking and double task fast walking ($P<0.05$). However, it was not statistically significant for double task habitual walking.[92] Another RCT concluded that EA add-on stimulation treatment to conventional treatment markedly improves quality of life for patients with Parkinson's.[93] Another RCT, consisting of a small sample size (n=15 cases, 1:2 case/control randomization), contributed that center-of-gravity sway to anterior-posterior sway was reduced by 31% and ankle-hip sway reduced by 46% significantly compared to no change in the sham treatment group ($p<0.02$). The clinical rating revealed an overall improvement ($p < 0.01$) in mentation, behavior, and mood (Unified Parkinson Disease Rating Scale (UPDRS) part I, 49%), activities of daily living (UPDRS part II, 46%), and motor examination (UPDRS part III, 40%). There was a significant reduction ($p < 0.02$) in the specific items regarding UPDRS fall status (67%) and rigidity (48%).[62] Due to the paucity of evidence presented, conclusions cannot be drawn.

Acute Cerebral Infarction

One RCT focused on patients with acute ischemic cerebral apoplexy and results suggested that EA stimulation treatment was more significantly effective compared to control for NIHSS at 4 week but became statistically non-significant at 12 weeks.[12] This single study did not provide sufficient data to draw conclusions about the effectiveness of EA stimulation for this indication.

Fibromyalgia

In one RCT study of patients with fibromyalgia, the authors reported reduced BPI severity to a greater extent over eight weeks within patients receiving EA stimulation compared to mock laser (ML) treatment (EA stimulation = -1.14, ML= -0.46, p=0.036). Participants receiving EA stimulation, as compared to ML, also displayed increased resting functional connectivity between the primary somatosensory cortical representation of the leg. Increases in aINS gamma-

aminobutyric acid (GABA+) were associated with reductions in pain severity (GABA+(i.u.): r(16)=-0.59, P=0.01). Authors concluded that the somatosensory component of acupuncture modulates primary somatosensory functional connectivity in association with insular neurochemistry to reduce pain severity in fibromyalgia.[58]

Carpal Tunnel Syndrome

Only one RCT evaluating EA stimulation in carpal tunnel syndrome was identified. The authors reported that in patients with mild-to-moderate carpal tunnel syndrome, mean scores of pre-post symptom VAS decreased significantly statistically (P<0.05) for the EA stimulation treatment group compared to the night-splinting group.[94] There were no significant differences between the groups in pre-post symptom severity scales or functional improvement scales. This same RCT was cited in an SLR of carpal tunnel syndrome interventions.[95] There is insufficient evidence from this study to draw any conclusions.

Fatigue

Of the selected studies, two meta-analyses and two RCTs evaluated EA stimulation treatment effectiveness for fatigue. The authors reported that EA stimulation could have a significant effect in treating fatigue.[96-99] One meta-analysis publication reported that EA stimulation showed statistically more effectiveness in reducing cancer-related fatigue than sham electroacupuncture (SMD -0.85, 95% CI=-1.44~-0.27, P = 0.004).[96] Results of the other meta-analysis suggested that EA stimulation treatment reduced fatigue 2 to 20% with an absolute reduction of 11% on a 10 point scale.[97] One RCT of patients with non-small cell lung cancer found that transcutaneous electrical acupoint stimulation (TEAS) had a statistically significant effect in treating behavioral, effective, and cognitive fatigue by the Revised Piper Fatigue Scale compared to sham EA stimulation treatment (P<0.05).[98] In the second RCT, the authors found statistically significant differences between the TEAS treatment group and sham treatment groups for treatment of fatigue (P<0.05).[99]

Headache/Migraine

One meta-analysis and two RCs evaluated EA stimulation treatment for headaches. The meta-analysis showed EA stimulation treatment to be more efficacious than manual acupuncture in treating patients with tension-type headaches (SMD - 0.13, 95% CI=-0.41~0.14, P=0.001).[96] The results of an RCT of chronic tension-type headache showed that EA stimulation treatment was statistically superior to sham treatment in alleviating headache pain (P<0.05).[100] An RCT evaluating EA stimulation treatment for migraine showed a better response in patients with migraine compared to a drug treatment group based on patient responses to the World Health Organization Quality of Life Biomedical Research and Education assessment and the Migraine Disability assessment.[101] While what is published so

far shows favorable results for EA stimulation to treat headache and migraine, additional studies are needed.

5.5 Overall Literature Review Conclusions

The majority of publications (77/105; 73%) did not report adverse events (AEs) or safety risks with the use of electroacupuncture. Of the 17 studies reporting AEs, the most serious AEs were 3 cases of death. These deaths were identified in a recent SLR of case series and reports, and a limitation was that the original case series detailing the deaths was a Chinese journal article published in 1981 about which little detail was available in regard to clinical practice or IRB oversight. The three most frequently reported AEs were exacerbation of CINV, skin pallor and skin pigmentation. The limitations to interpreting device effectiveness for the indications selected are 1) small sample sizes as only 28% (30/105) of the literature had sample sizes over 100 patients, and 2) the indication of pain was evaluated primarily using VAS or NPRS, which are subjective in nature. In the published literature, the evidence strongly indicates EA stimulation treatment has a favorable effect on musculoskeletal, post-operative, neuropathic pain, and analgesic reduction compared to sham and control groups (conventional treatment or no treatment). For neurological and muscular indications, there is evidence that EA stimulation treatment may be favorable for treating stroke. For stroke rehabilitation, Parkinson's disease, acute cerebral infarction, carpal tunnel syndrome, fatigue, and headache/migraine indications, there is weak or conflicting evidence and additional studies are required to draw conclusions. Published evidence is sparse and additional studies are also required for the use of EA stimulation treatment for fibromyalgia, post-operative nausea/vomiting and motion sickness. There was no published evidence for use of EA stimulation in visceral pain, Bell's Palsy, or chronic fatigue syndrome.

In summary, more evidence is needed to determine whether the usage of EA stimulation is consistently associated with the AE events reported and whether there is strong evidence of EA stimulation effectiveness in musculoskeletal, post-operative, neuropathic pain, analgesic reduction, and stroke indications. There is little published evidence and additional studies are needed to draw conclusions about EA stimulation treatment for stroke rehabilitation, Parkinson's disease, acute cerebral infarction, carpal tunnel syndrome, fatigue, fibromyalgia, and headache. No published evidence exists within the study inclusion criteria for visceral pain, Bell's Palsy, or chronic fatigue syndrome. All of these indications require further study.

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: Electro-Acupuncture Stimulator (Product Code BWK)

Individual MDRs for electro-acupuncture stimulators 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 Reports (MDR) database on March 9, 2021 to identify adverse events related to the use of Electro-Acupuncture Stimulator devices (Product Code BWK) entered between April 3, 1979 and December 31, 2020. The search did not identify any relevant MDRs electro-acupuncture stimulator devices.

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: Electro-Acupuncture Stimulators

The FDA conducted queries of the Medical Device Recall database on May 5, 2021, to identify recalls related to electro-acupuncture stimulators (product code BWK). The search was not timeframe restricted and included all recalls reported under product code BWK. The search did not identify any relevant recalls for electro-acupuncture stimulators.

8. Summary

In light of the information available, the Panel will be asked to comment on whether electro-acupuncture stimulators under product codes "BWK" 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;

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 electro-acupuncture stimulators. The 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 electro-acupuncture stimulators

Identified Risk	Recommended Mitigation Measure
Adverse tissue reaction	• Biocompatibility evaluation • Labeling
Infection	• Sterilization validation • Cleaning validation • Shelf life testing • Labeling
Patient injury or discomfort, including: • electrical shock or burn • bleeding	• Electrical, mechanical, and thermal safety testing • Electromagnetic compatibility (EMC) testing • Non-clinical performance testing • Software validation, verification, and hazard analysis • Labeling
Use error	• Labeling

The Panel will be asked whether this list is a complete and accurate list of the risks to health presented for electro-acupuncture stimulators 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 electro-acupuncture stimulators under product code "BWK":

1. The patient-contacting components of the device must be demonstrated to be biocompatible.
2. Performance testing must demonstrate the sterility of device components that are provided sterile.
3. Performance testing must demonstrate continued sterility, package integrity, and device functionality over the labeled shelf life for device components provided sterile.

4. Performance testing must validate cleaning procedures and demonstrate continued device functionality over the labeled shelf life for reusable patient-contacting components.
5. Performance testing must demonstrate electromagnetic compatibility and electrical, mechanical and thermal safety in the intended use environment.
6. Non-clinical performance testing of the device and electrodes must be conducted to validate the specified electrical output and duration of stimulation of the device.
7. Software verification, validation, and hazard analysis must be performed.
8. Labeling must include the following:
    a. Instructions for use, including identification and placement of appropriate electrodes, and the typical sensations experienced during treatment;
    b. A warning stating that the device is only for use on clean, intact skin;
    c. A detailed summary of the electrical output and the device technical parameters;
    d. A shelf life for the device and accessories;
    e. A statement that sterile components are intended for single use only; and
    f. Instructions on care and cleaning of the device for reusable components.

If the panel believes that Class II is appropriate for electro-acupuncture stimulators under product code "BWK," 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 electro-acupuncture stimulators indicated for use in the practice of acupuncture be regulated as Class II devices.

882.5889 Electro-acupuncture stimulator.

(a) Identification.

An electro-acupuncture stimulator is a prescription device intended for medical purposes, such as pain relief, that is used to apply an electrical current to acupuncture points through electrodes in the practice of acupuncture by a qualified practitioner of acupuncture therapy.

(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. Performance testing must demonstrate the sterility of device components that are provided sterile.
3. Performance testing must demonstrate continued sterility, package integrity, and device functionality over the labeled shelf life for device components provided sterile.
4. Performance testing must validate cleaning procedures and demonstrate continued device functionality over the labeled shelf life for reusable patient-contacting components.
5. Performance testing must demonstrate electromagnetic compatibility and electrical, mechanical and thermal safety in the intended use environment.
6. Non-clinical performance testing of the device and electrodes must be conducted to validate the specified electrical output and duration of stimulation of the device.
7. Software verification, validation, and hazard analysis must be performed.
8. Labeling must include the following:
    g. Instructions for use, including identification and placement of appropriate electrodes, and the typical sensations experienced during treatment;
    h. A warning stating that the device is only for use on clean, intact skin;
    i. A detailed summary of the electrical output and the device technical parameters;
    j. A shelf life for the applicators and components provided sterile;
    k. A statement that sterile components are intended for single use only; and
    l. Instructions on care and cleaning of the device for reusable components.

Based on the available scientific evidence, the FDA will ask the Panel for their recommendation on the appropriate classification of electro-acupuncture stimulators under product code "BWK."

Appendix A: Literature Search Terms and Filters for Electro-Acupuncture Stimulators

FDA conducted a literature search to identify any relevant references published between January 1, 2010 and December 31, 2020. We searched two electronic databases, PubMed and Embase. Multiple searches were conducted using product names, related terminologies, combined with brand names without the limitation of indication of use. Articles were then selected based on specific indications shown below.

- Pain
  - Musculoskeletal pain
  - Post-operative pain
    - Analgesic Reduction
  - Neuropathic Pain
  - Visceral Pain

- All neurological conditions and muscular conditions listed below:
  - Stroke
  - Bell's palsy
  - Spastic Cerebral Palsy
  - Epilepsy
  - Parkinson’s Disease
  - Acute cerebral infarction
  - Fibromyalgia
  - Stroke rehabilitation
  - Carpal tunnel syndrome
  - Lumbar spinal stenosis
  - Fatigue/chronic fatigue syndrome
  - Paresthesia
  - Headache/Migraine

The highest-level evidence papers (RCTs and meta-analysis using RCTs) were extracted for device effectiveness, and all types of studies including case reports were extracted for device adverse events. A total of 2,953 references was identified after combining the results for the search terms used in PubMed and Embase. The search syntaxes are below:

***PubMed Search Syntax*:**

(1) ((electro acupuncture stimulator) or electroacupuncture) and ("2010/01/01"[pdat] : "2020/12/31"[pdat] and english[lang]) and "humans"[mesh terms] and hasabstract[text]
(2) ((electro acupuncture stimulator) OR electroacupuncture) and ("2010/01/01"[pdat] : "2020/12/31"[pdat] and english[lang]) AND hasabstract[text] NOT Medline[SB]

(3) ((electrical stimulation AND acupoint) OR (electrical acustimulation)) and ("2010/01/01"[pdat] : "2020/12/31"[pdat] and english[lang]) and "humans"[mesh terms] and hasabstract[text]
(4) ((electrical stimulation AND acupoint) OR (electrical acustimulation)) and ("2010/01/01"[pdat] : "2020/12/31"[pdat] and english[lang]) AND hasabstract[text] NOT Medline[SB]
(5) Reliefband OR "Relief Band"
(6) Ansistim

Embase Search Syntax:

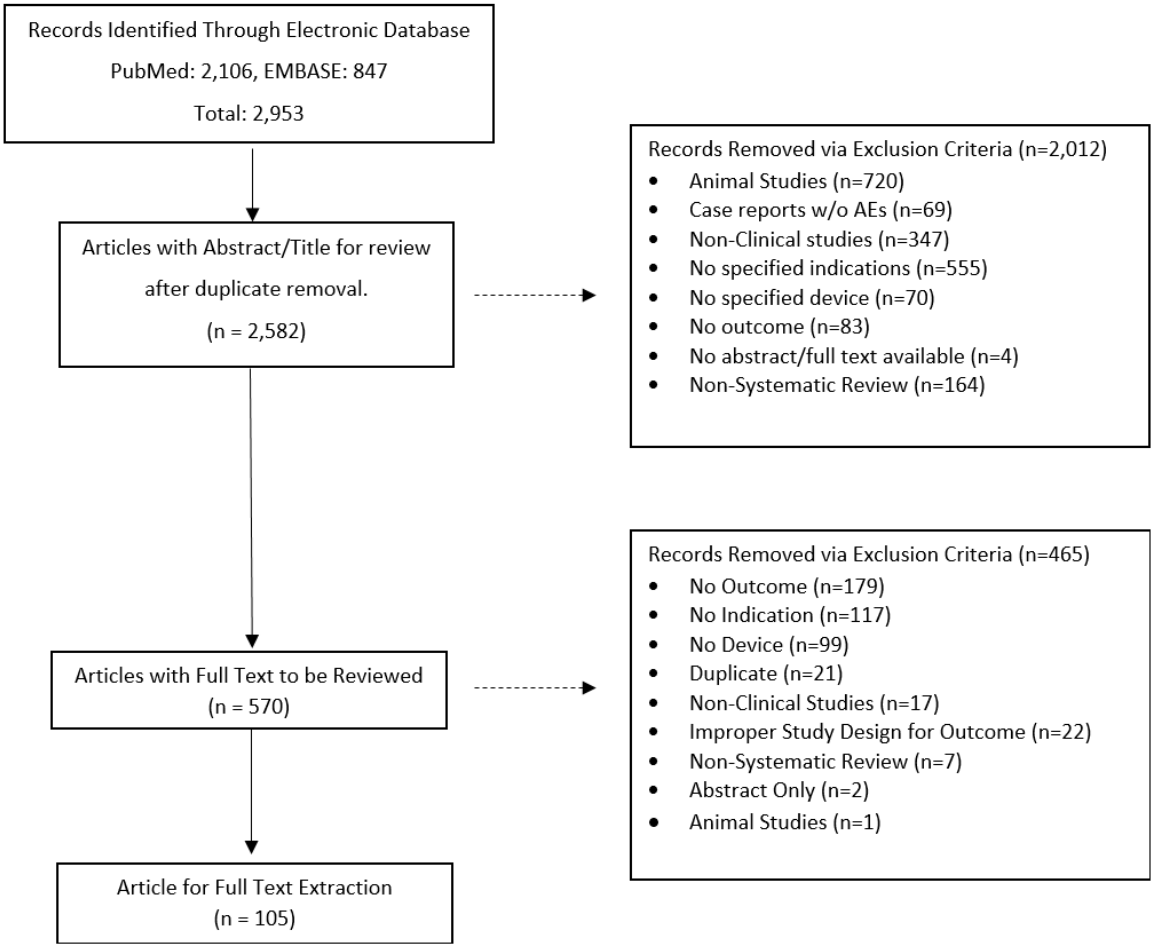
(1) (('electroacupuncture'/exp OR electroacupuncture:ti,ab OR 'acupuncture, electric':tn,ti,ab OR 'electric acupuncture':tn,ti,ab OR 'electroacupuncture':tn,ti,ab) AND [english]/lim AND [abstracts]/lim AND [2010-2020]/py) AND ('clinical article'/de OR 'clinical trial'/de OR 'clinical trial topic'/de OR 'comparative effectiveness'/de OR 'comparative study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'evidence based medicine'/de OR 'evidence based practice'/de OR 'feasibility study'/de OR 'human'/de OR 'intention to treat analysis'/de OR 'major clinical study'/de OR 'meta analysis'/de OR 'meta analysis topic'/de OR 'normal human'/de OR 'parallel design'/de OR 'pilot study'/de OR 'prospective study'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial topic'/de OR 'retrospective study'/de OR 'systematic review'/de OR 'systematic review topic'/de) AND ('article'/it OR 'article in press'/it OR 'conference paper'/it OR 'conference review'/it OR 'review'/it) AND ('abdominal pain'/dm OR 'adverse event'/dm OR 'allodynia'/dm OR 'alzheimer disease'/dm OR 'anxiety disorder'/dm OR 'barthel index'/dm OR 'brain ischemia'/dm OR 'carpal tunnel syndrome'/dm OR 'cerebrovascular accident'/dm OR 'chronic disease'/dm OR 'chronic pain'/dm OR 'depression'/dm OR 'dizziness'/dm OR 'dyspepsia'/dm OR 'faintness'/dm OR 'fatigue'/dm OR 'fibromyalgia'/dm OR 'headache'/dm OR 'insomnia'/dm OR 'knee osteoarthritis'/dm OR 'low back pain'/dm OR 'migraine'/dm OR 'nausea'/dm OR 'nausea and vomiting'/dm OR 'neck pain'/dm OR 'neuropathic pain'/dm OR 'pain'/dm OR 'paresthesia'/dm OR 'peripheral neuropathy'/dm OR 'postoperative pain'/dm OR 'shoulder pain'/dm OR 'side effect'/dm OR 'sleep disorder'/dm OR 'vomiting'/dm)
(2) 'es-130' AND [2010-2020]/py AND [humans]/lim AND [english]/lim AND [abstracts]/lim
(3) 'p stim' AND [2010-2020]/py AND [humans]/lim AND [english]/lim AND [abstracts]/lim
(4) (reliefband:dn OR reliefband/dn OR reliefband:ti OR reliefband:ab) AND [2010-2020]/py AND [humans]/lim AND [english]/lim AND [abstracts]/lim

Study Selection Process:

The articles identified from PubMed and EmBase search were screened and reviewed for eligibility to be included in the review. The abstracts/titles were first screened to remove

irrelevant articles and to identify articles to be reviewed in full text. The full text articles were reviewed and assessed in detail regarding their eligibility for inclusion/exclusion and the study results. The full diagram of article retrieval and selection are detailed in Appendix B.

Appendix B: Flow Diagram of Systematic Literature Review Search Results



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Classification of Electro-Acupuncture Stimulators
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 electro-acupuncture stimulators:

Identified Risk	**Description/Examples**
Adverse tissue reaction	• Skin irritation • Local pain • Changes in skin pigmentation such as hematoma and skin pallor
Infection	• Infection due to non-sterile/contaminated needle and other types electrodes that enters epidermis or deeper layer of the skin • Sepsis
Patient injury or discomfort: including: • electrical shock or burn • bleeding	• Excessive trauma, perforation of blood vessels and organs caused by needles leading to bleeding, ecchymosis, hematoma • Electrical shock or burn • Muscle cramping
Use error	• User discomfort, tissue injury, or delayed treatment

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of electro-acupuncture stimulators under product code "BWK". In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these electro-acupuncture stimulators.

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 electro-acupuncture stimulators. 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 electro-acupuncture stimulators under product code "BWK"

Identified Risk	**Recommended Mitigation Measure**
Adverse tissue reaction	• Biocompatibility evaluation • Labeling
Infection	• Sterilization validation • Cleaning validation • Shelf life testing • Labeling
Patient injury or discomfort: including: • electrical shock or burn • bleeding	• Electrical, mechanical, and thermal safety testing • Electromagnetic compatibility (EMC) testing • Non-clinical performance testing • Software validation, verification, and hazard analysis • Labeling
User error	• Labeling

Please discuss whether the identified special controls for electro-acupuncture stimulators 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. Performance testing must demonstrate the sterility of device components that are provided sterile.
3. Performance testing must demonstrate continued sterility, package integrity, and device functionality over the labeled shelf life for device components provided sterile.
4. Performance testing must validate cleaning procedures and demonstrate continued device functionality over the labeled shelf life for reusable patient-contacting components.
5. Performance testing must demonstrate electromagnetic compatibility and electrical, mechanical and thermal safety in the intended use environment.
6. Non-clinical performance testing of the device and electrodes must be conducted to validate the specified electrical output and duration of stimulation of the device.
7. Software verification, validation, and hazard analysis must be performed.
8. Labeling must include the following:
    a. Instructions for use, including identification and placement of appropriate electrodes, and the typical sensations experienced during treatment;
    b. A warning stating that the device is only for use on clean, intact skin;
    c. A detailed summary of the electrical output and the device technical parameters;
    d. A shelf life for the device and accessories;
    e. A statement that sterile components are intended for single use only; and
    f. Instructions on care and cleaning of the device for reusable components.

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