Public Workshop
Neurodiagnostics and Non-Invasive Brain Stimulation Medical Devices
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Office of Compliance Reorganization

CDRH Office of Compliance

- Division of Manufacturing and Quality
- Division of International Compliance Operations
- Division of Premarket and Labeling Compliance
  - Division of Analytics and Program Operations
  - Division of Bioresearch Monitoring
DPLC Responsibilities

- Enforcement of regulations related to:
  - the submission of premarket applications and
  - labeling requirements
    - including promotion and advertising materials and practices

- Jurisdictional Determinations
  - Device Determinations
  - Preamendments Determinations

- Custom Device Program
  - Annual Report Reviews
Division of Premarket and Labeling Compliance

Jurisdictional Officer

Division of Premarket and Labeling Compliance

Surveillance and Enforcement Branch I
- Cardiovascular
- General and Plastic Surgery
- Anesthesiology
- General Hospital
- Obstetrics and Gynecology
- Gastro-Urology
- Respiratory

Regulatory Counsel

Surveillance and Enforcement Branch II
- Dental
- Ear, Nose, and Throat
- Neurology
- Ophthalmological
- Orthopedics
- Physical Medicine
DPLC PRIORITIES
IMPACT-Based Priorities

- Understand scope of clearance and approval - coordinate with ODE/OSB/OCE

- Focus on resolution of violations or issues not taking “action”
  - Meaningful, Timely

- Use of non-enforcement actions (outreach) to resolve less significant issues
  - Proportional, Timely

- Consider All-at-Once rather than One-at-a-Time strategies
  - Informed, Proportional, Consistent
CDRH Authority

- Labeling for all devices
- Advertising for restricted devices
- Labeling is broad category
- Federal Trade Commission has jurisdiction over advertising of non-restricted devices and non-prescription drugs
Restricted Device Advertising

- 502(q) - misbranding for false or misleading advertising
- 502(r) - misbranding for failure to include statement of intended uses and risk
- Advertising not defined but 502(r) provides that it is printed material that FDA has not defined as labeling
- Restricted device area often misunderstood (restricted/prescription - statutory language and drugs language add to complication)
Common Problems

- **Third Party Sellers** (claims, lack of prescription, device quality, post-recall)
- **Claims regarding the latest crisis**
  - Outbreaks, Natural Disasters (H1N1, Japan tsunami)
- **Breaking commitments made during the premarket review process** (changes use, affects trust level)
- **Exceeding boundaries of enforcement discretion**
  - Mobile Medical Apps
  - 513(g)
- **Misuse of exempt product classifications**
Unapproved Uses (off-label)

- For devices, complicated by general/specific uses and indications
  - soft tissue ablation v. atrial fibrillation
  - Removing tissue v. treating cancer

- Some clearly changes in use
  - Temporary increase in clear nail v. treating onychomycosis infection (misleading, probably not harmful)
  - Bone growth protein in cervical spine when approved for thoracic spine (fatal outcomes)
  - Dermal filler mentioned above
Practitioners’ Promotion of Medical Devices

- Section 1006 (formerly §906) of Act allows, in course of legitimate patient/practitioner relationship, unapproved indications or uses of approved devices but does not provide new permissions to promote those uses. (Emphasis added and specific to devices.)

- Complicated relationships among practitioners, user facilities, academic centers, companies

- Products considered “held for sale”
Practitioner Promotion

• Numerous practitioners promote unapproved uses and provide no risk information

• Company involvement varies
  - Companies generally do not appear to constrain promotion and sometimes encourage or invite it
  - Some companies do express concern about off label use and promotion by others because of risk to patients or potential product liability

• Different from drug advertising - healthcare practitioners don’t commonly independently promote drugs (some practitioners do promote dietary supplements)
Practitioner Promotion

- **Thermography**
  - Digital infrared light cleared as Class II “adjunct” to screening
  - Clinics changed intended use to “diagnostic” screening by claiming thermography was substitute for and superior to mammography for detection of breast cancer

- **1-800-Get-Thin**
  - Chain of California clinics advertising gastric banding surgery with Allergan’s LapBand
    - made misleading claims (502(q))
    - No risk information in violation of 502(r)

- [http://www.fda.gov/forconsumers/consumerupdates/ucm279301.htm](http://www.fda.gov/forconsumers/consumerupdates/ucm279301.htm)
Practitioner Promotion

- LASIK (Laser Assisted in Situ Keratomileusis)
- [http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/default.htm](http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/default.htm)
- Many websites promoting specific lasers and not only “outcomes” or services so within FDA jurisdiction
- Excimer lasers are Class III restricted and prescription devices
- Multiple approaches
  - Open letters to practitioners
  - Letters to ASCRS and AAO advising of problem
  - Warning letters to specific practitioners as last effort
    - Some positive results
Preapproval Promotion

- Investigational Devices
  - Section 812.7 prohibits promotion of investigational devices as safe and effective for use being tested
  - Adulterated - violation of 501(i)
  - Pending 510(k) submission
    - CPG 300.600

- Pending PMA
  - Not included in CPG
Comparative Claims

- 21 CFR 801.6 - a product is misbranded if the labeling makes misleading comparison between it and another FDA-regulated product (drug, food, cosmetic)
- CDRH requires head to head trials, and it is misleading to compare data from multiple studies
- Performance claims may not change intended use but still affect veracity of labeling
- Substantially equivalent does not mean “much better than the predicate”
- Safe and effective does not mean “safer and more effective”
Combination Products

- Combination products are defined in 21 CFR 3.2(e). The term combination product includes:
  - (1) A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
  - (2) Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products;
Combination Products

- (3) A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or

- (4) Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.
Combination Products

- Contrast agents/Imaging devices
  - One contrast agent contraindicated for cardiac perfusion but promotion of device software for cardiac imaging

- Diagnostic tests/drug efficacy (personalized genomic supported medicine)

- Centers work closely with Office of Combination Products to address primary mode of action (PMOA) questions and with each other to reach best resolution
Combination Products

- 201(g) - drug - (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any articles specified in clause (A), (B), or (C).

- 201(h) - device - same except framed as negative -
  - “...an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, ...
  - does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.
  - [http://www.fda.gov/RegulatoryInformation/Guidances/ucm258946.htm](http://www.fda.gov/RegulatoryInformation/Guidances/ucm258946.htm)
Combination Products

- **PharmaJet - 2011-2014**
  - Needleless jet injector used nationwide to administer influenza vaccine
  - CDRH had cleared device for use “with drugs and vaccines” and with no explicit limitation
  - CBER had approved for administration without syringe and needle was only the measles, mumps, rubella (MMR) vaccine
  - FDA issued public safety notice
  - 2014 - first **limited** approval of influenza vaccine specifically for administration with injector (ages 18-64)
  - Drug/biologic/device manufacturers should be aware of potential problems
Combination Products

- Drug-eluting stent - CDRH lead Center - PMOA stent
- Metered dose inhalers - CDER lead - PMOA drug
- Wound products
  - Products cleared as devices with preservative sufficient to maintain sterility in bottle but marketed with drug antimicrobial claims to treat HIV, MRSA, SARS, H1N1- query misbranded device or new drug claims or both
  - Bandages with silver, copper, other additives, cleared to prevent microbial growth in bandage but promoted to reduce infection in wound - same issues about misbranded device or new drug claims or both
Marketed Devices

• DEN140029 - Cognivue
  - this was a recent de novo for a battery of cognitive tests to *aid in the assessment* of cognitive function.
    • *Not* to diagnose any particular condition or as a standalone assessment tool

• K141865 - DANA
  - cleared under product code LQD as a *tool that provides an objective measurement of reaction time*. 
Marketed Devices

- K133382, K122149, K040894 - QbTest
  - Measures head motion
  - Measures performance on various cognitive tasks
    - to *provide objective measurements* of
      - hyperactivity,
      - impulsivity, and
      - inattention
    - to *aid in the clinical assessment* of ADHD
Possible Concerns

- Diagnostic claims
- Standalone claims
- Evaluation of impact of pharmaceutical treatment
- Concerns about measurement at one moment in time used to identify changing conditions
- Use in inappropriate populations
- Claims by practitioners, clinics, schools
Outreach/Enforcement

• Consider scope of promotion
• Evaluation sponsor and practitioner roles in false or misleading claims or claims that change intended use
• Public statements if necessary
Recent Grounds for First Amendment Considerations

- **Citizen Petitions from Medical Information Working Group**
  - (1) responses to unsolicited requests;
  - (2) scientific exchange;
  - (3) communications to formulary committees, payors, and similar entities; and
  - (4) dissemination of third-party clinical practice guidelines that discuss off-label use.

- **Litigation**
  - Sorrell v. IMS Health, Inc., 131 S. Ct. 2653 (2011) (prescribing data leased or sold to pharmaceutical companies)
  - United States v. Caronia, 703 F.3d 149 (2d Cir. 2012) (false and misleading)
  - Amarin, Pacira (CDER)
DPLC Contact Information

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