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HOGAN & HARTSON L.L.P.

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June 11, 2001

BY HAND DELIVERY

Food and Drug Administration
Center for Medical Devices and Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850

Attn.: Dr. Jeffrey Cooper (HFZ-470)

Re: Request for Evaluation of Automatic Class III Designation for Given Imaging Ltd. Premarket Notification K010312 - Given® Diagnostic Imaging System ("Given System")

Dear Dr. Cooper:

In accordance with Section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act ("FDC Act"), Given Imaging Ltd. ("Given" or the "company") is submitting the enclosed request for evaluation of automatic class III designation for the company's Given® Diagnostic Imaging System ("Given System"). The purpose of this request is to seek classification of this product by the Food and Drug Administration ("FDA") as a class II medical device. The general controls and special controls that Given proposes for such products are described in detail in the attached submission as described in the agency's guidance document entitled, "New Section 513(f)(2) – Evaluation of Automatic Class III Designation, Guidance for Industry and Staff." The information contained in this submission was provided to Hogan & Hartson, L.L.P., by Given for submission to FDA, and Given is solely responsible for the accuracy and completeness of this information.

Ingestible telemetric video diagnostic imaging systems are ingestible devices used to capture and transmit via telemetric transmission video images of hollow organs, canals, and mucosal tissues. Ingestible telemetric video diagnostic imaging systems are intended for the detection of pathologies as an adjunctive tool in the diagnosis of gastrointestinal disorders and diseases. We trust that the information contained in the enclosed request for evaluation will be sufficient to

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enable FDA to classify ingestible telemetric video diagnostic imaging systems as class II medical devices subject to special controls for the specified intended uses. If you have any questions regarding this request for evaluation, please do not hesitate to contact me at (202) 637-5794.

Sincerely yours,

Jonathan S. Kahan

Attachment

cc: Gavriel Meron, Given Imaging, Ltd.
Shoshana Friedman, Push-Med, Ltd.
Janice M. Hogan, Esq.
Randy J. Prebula

CDRH Submission Cover Sheet

Date of Submission:	FDA Document Number:
June 11, 2001	

Section A — Type of Submission

PMA	PMA Supplement	PDP	510(k)	Meeting
☐ Original submission ☐ Modular submission ☐ Amendment ☐ Report ☐ Report Amendment	☐ Regular ☐ Special ☐ Panel Track ☐ 30-day Supplement ☐ 30-day Notice ☐ 135-day Supplement ☐ Real-Time Review ☐ Amendment to ☐ PMA Supplement	☐ Presubmission summary ☐ Original PDP ☐ Notice of intent to start clinical trials ☐ Amendment to PDP Report	☐ Original submission: Traditional ☐ Special ☐ Abbreviated ☐ Additional information: ☐ Traditional ☐ Special ☐ Abbreviated	☐ Pre-IDE meeting ☐ Pre-PMA meeting ☐ Pre-PDP meeting ☐ 180-day meeting ☐ Other (specify)

IDE	Humanitarian Device Exemption	Class II Exemptions	Evaluation of Automatic Class III Designation	Other Submission
☐ Original submission ☐ Amendment ☐ Supplement	☐ Original submission ☐ Amendment ☐ Supplement ☐ Report	☐ Original submission ☐ Additional information	☒ Original Submission ☐ Additional information	Describe Submission:

Section B — Applicant or Sponsor

Company / Institution Name:	Establishment Registration Number:
Given Imaging Ltd.	9044616
Division Name (if Applicable):	Phone Number (include area code): 011 972 4 909 7789
Street Address: Building 7, New Industrial Park, P.O. Box 258	FAX number (include area code): 011 972 4 959 2466

City:	State / Province:	Country:
Yoqneam 20692		Israel

Contact Name:	
Gavriel Meron	
Contact Title: President and CEO	Contact e-mail address: gabim@givenimaging.com

Section C — Submission Correspondent (if different from above)

Company / Institution Name:	Establishment Registration Number:
Hogan & Hartson L.L.P.	Not applicable
Division Name (if Applicable):	Phone Number (include area code): (202) 637-5794
Street Address: 555 Thirteenth Street, N.W.	FAX number (include area code): (202) 637-5910

City:	State / Province:	Country:
Washington	D.C.	U.S.A.

Contact Name: Jonathan S. Kahan, Esq.	
Contact Title: Regulatory Counsel	Contact e-mail address: JSKahan@hhlaw.com

Section D1	Reason for Submission – PMA, PDP, or HDE	
☐ New device ☐ Withdrawal ☐ Additional or expanded indications ☐ Licensing agreement ☐ Process change ☐ Manufacturing ☐ Sterilization ☐ Packaging ☐ Other (specify) ☐ Response to FDA Correspondence: ☐ Request for applicant hold ☐ Request for removal of applicant hold ☐ Request for Extension ☐ Request to remove or add manufacturing site ☐ Other reason (specify):	☐ Change in design, component or specification: ☐ Software ☐ Color Additive ☐ Material ☐ Specifications ☐ Other (specify below) ☐ Labeling Changes ☐ Indications ☐ Instructions ☐ Performance Characteristic ☐ Shelf Life ☐ Trade Name ☐ Other (Specify below)	☐ Location Change ☐ Manufacturer ☐ Sterilizer ☐ Packager ☐ Distributor ☐ Report Submission ☐ Annual or Periodic ☐ Post-approval study ☐ Adverse Reaction ☐ Device Defect ☐ Amendment ☐ Change in Ownership ☐ Change in correspondent

Section D2	Reason for Submission – IDE	
☐ New device ☐ Addition of institution ☐ Expansion / extension of study ☐ IRB certification ☐ Request hearing ☐ Request waiver ☐ Termination of Study ☐ Withdrawal of application ☐ Unanticipated adverse effect ☐ Notification of emergency use ☐ Compassionate use request ☐ Treatment IDE ☐ Continuing availability request ☐ Other reason (please specify)	☐ Change in: ☐ Correspondent ☐ Design ☐ Informed consent ☐ Manufacturer ☐ Manufacturing process ☐ Protocol – feasibility ☐ Protocol – other ☐ Sponsor ☐ Report submission: ☐ Current investigator ☐ Annual progress ☐ Site waiver limit reached ☐ Final	☐ Response to FDA letter concerning: ☐ Conditional approval ☐ Deemed approved ☐ Deficient final report ☐ Deficient progress report ☐ Deficient investigator report ☐ Disapproval ☐ Request extension of time to respond to FDA ☐ Request meeting

Section D3	Reason for Submission – 510(k)	
☐ New device	☐ Change in technology	☐ Change in materials
☐ Additional or expanded indications	☐ Change in design	☐ Change in manufacturing process
☒ Other reason (specify): **Request for Evaluation of Automatic Class III Designation**		

Section E	Additional Information on 510(k) Submission			
Product codes of devices to which substantial equivalence is claimed:				Summary of, or statement concerning, safety and effectiveness data: ☐ 510(k) summary attached ☐ 510(k) statement
1.	2.	3.	4.	
5.	6.	7.	8.	

Information on devices to which substantial equivalence is claimed:

510(K) Number	Trade or proprietary or model name	Manufacturer
1.	1.	1.
2.	2.	2.
3.	3.	3.
4.	4.	4.
5.	5.	5.
6.	6.	6.

Section F	Product Information – Applicable to All Applications	
Common or usual name or classification name: **Ingestible Telemetric Video Diagnostic Imaging System**		
Trade or proprietary or model name		Model number
1. Given® Diagnostic Imaging System		1.
2.		2.
3.		3.
4.		4.
5.		5.

FDA document number of all prior submissions (regardless of outcome):

1. **K010312**	2.	3.	4.	5.	6.
7.	8.	9.	10.	11.	12.

Data included in submission: ☐ Laboratory Testing ☐ Animal trials ☐ Human trials

Section G	Product Classification – Applicable to All Applicants	
Product code: NEZ	C.F.R. Section: To Be Determined	Device Class: ☐ Class I ☐ Class II ☒ Class III ☐ Unclassified
Classification Panel: This device has been classified as a class III device pursuant to an NSE decision dated June 8, 2001		

Indications (from labeling):

Ingestible telemetric video diagnostic imaging systems are ingestible devices used to capture and transmit via telemetric transmission video images of hollow organs, canals, and mucosal tissues. Ingestible telemetric video diagnostic imaging systems are intended for the detection of pathologies as an adjunctive tool in the diagnosis of gastrointestinal disorders and diseases.

Given Imaging, Ltd.'s
Given® Diagnostic Imaging System
Request for Evaluation of
Automatic Class III Designation

Given Imaging Limited
Building 7, New Industrial Park
P.O. Box 258
Yoqneam 20692
Israel

TABLE OF CONTENTS

I. INTRODUCTION

The purpose of this request for evaluation of automatic class III designation is to request classification of Given Imaging, Ltd.'s ("Given" or the "company") Given® Diagnostic Imaging System as a class II medical device requiring special controls by the Food and Drug Administration ("FDA" or the "agency") in accordance with Section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act ("FDC Act").

The Given® Diagnostic Imaging System ("Given System") is comprised of the M2A® Capsule, a Data Recorder Set, and a Rapid™ Workstation. The System is intended for the detection of pathologies as an adjunctive tool in the diagnosis of small bowel gastrointestinal disorders and diseases. The Given System may be used in hospitals, outpatient clinics, and physician offices. After the M2A® Capsule is swallowed, the patient is not restricted to a medical environment.

As discussed in greater detail in this request for de novo classification as a class II medical device, Given submitted a 510(k) notice for the Given System on February 1, 2001. On June 8, 2001, Given received a letter from FDA indicating that the agency had determined that the Given System, a ingestible telemetric video diagnostic imaging system intended for the detection of pathologies as an adjunctive tool in the diagnosis of small bowel gastrointestinal disorders and diseases, was not substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, or to any device which has been reclassified into class I (General Controls) or class II (Special Controls), due to the differences in technological characteristics between the legally marketed preamendments devices and the Given System (see **Attachment 1**). That letter indicated, however, that the device might be a candidate for Evaluation of Automatic Class III Designation.

II. NAME OF DEVICE

A. Trade or Proprietary Name

Given® Diagnostic Imaging System

B. Common Name

Ingestible Telemetric Video Endoscopy System, Ingestible Telemetric Video Diagnostic Imaging System

C. Classification Names

FDA classified this product as a class III medical device on June 8, 2001. The classification name has not yet been established.

D. Product Codes

Not Yet Determined

E. 510(k) Number Under Which the Device Was Found Not Substantially Equivalent

K010312

III. STATEMENT OF CROSS REFERENCE TO ORIGINAL 510(K)

In evaluating this request for evaluation of automatic class III designation, Given authorizes cross reference to and incorporates by reference all information contained within 510(k) notice K010312, submitted to FDA on February 1, 2001, and additional information pertaining to the 510(k) notice submitted to FDA between February 1, 2001, and May 3, 2001.

IV. RECOMMENDED CLASSIFICATION UNDER SECTION 513

Given recommends that ingestible telemetric video diagnostic imaging systems be classified as a class II medical device requiring special controls as described in greater detail in section VI, below.

Given further proposes the following device description for inclusion in the Code of Federal Regulations for ingestible telemetric video diagnostic imaging systems:

> "Ingestible telemetric video diagnostic imaging systems are ingestible devices used to capture and transmit via telemetric transmission video images for the inspection of hollow organs, canals, and mucosal tissues. Ingestible telemetric video diagnostic imaging systems are intended for the detection of pathologies as an adjunctive tool in the diagnosis of gastrointestinal disorders and diseases "

V. POTENTIAL BENEFITS AND RISK ANALYSIS

A. Potential Benefits

Current methods for examining the small bowel for the detection of pathologies as an adjunctive tool in the diagnosis of gastrointestinal disorders and diseases primarily include barium x-rays, and enteroscopy. However, the diagnostic value of these tests for a wide variety of specific lesions is low. Enteroscopy is a method to perform direct visual inspection of the small bowel mucosa beyond the reach of standard upper endoscopes. The procedure can be accomplished by examination with either push or sonde type endoscopes, or operative enteroscopy. Enteroscopy of the small intestine is difficult, requires a lengthy examination time, can only partially visualize the small intestine, is extremely uncomfortable, poses the risk of gastrointestinal perforation, and is not performed on a widespread basis.

Given believes that the current diagnostic methods are unsatisfactory, and there is thus a clear need for an adjunctive diagnostic tool that will be relatively comfortable for the patient, easy to use by the gastroenterologist, inexpensive, and can provide a reasonable level of visual screening and detection of small bowel abnormalities. In response to this perceived need, the company has developed the Given® Diagnostic Imaging System as an ingestible telemetric video diagnostic imaging system that provides for the telemetric transmission of video images by means of the M2A® Capsule, the Data Recorder Set, and the Rapid™ Workstation.

Classification of ingestible telemetric video diagnostic imaging systems as a class II medical device for the indication of the detection of pathologies as an adjunctive tool in the diagnosis of small bowel gastrointestinal disorders and diseases will provide the benefit of devices capable of rapid visualization and detection of pathologies using telemetric transmission of captured images in combination with the safe transmission of such images through conformance with various special controls described in the original 510(k) notice, K010312, and this request for evaluation.

B. Potential or Anticipated Risks

Given believes that the potential or anticipated risks associated with ingestible telemetric video diagnostic imaging devices may include: (1) biocompatibility; (2) electrical safety; (3) electromagnetic compatibility, interference, and radio frequency ("RF") propagation transmission power; (4) environmental interference with video image acquisition (*i.e.*, obscured optical pathway); (5) functional reliability (video unit integrity, battery life, illumination, field of view) and motility during passage through the gastrointestinal system; and (6) appropriate medical review of the captured images. Each of these potential or anticipated risks is addressed by the proposed special controls outlined below.

VI. PROPOSED GENERAL AND SPECIAL CONTROLS

A. General Controls

Given recommends that the Given system and other devices intended for the detection of pathologies as an adjunctive tool in the diagnosis of gastrointestinal disorders and diseases be subject to general controls, including the following sections of the FDC Act: (1) Section 501(adulteration); (2) Section 502 (misbranding); (3) Section 510 (registration); (4) Section 516 (banned devices); (5) Section 518 (notification); (6) Section 519 (records and reports); and (7) Section 520 (good manufacturing practices and general provisions).

B. Special Controls

Performance standards under Section 514 of the Federal Food, Drug, and Cosmetic Act have not been established for ingestible telemetric video diagnostic imaging devices. However, FDA established special controls for endoscopes and enteroscopes that are analogous or identical to tests that are routinely performed to assess the safety and effectiveness of Given's device. In addition, voluntary standards exist regarding electrical safety and electromagnetic interference that provide additional special controls regarding the performance of telemetric video diagnostic imaging systems. Finally, controlled animal and human clinical testing demonstrate that the video image acquisition system: (1) is not adversely affected by the ingestion process or the gastrointestinal environment; (2) functions reliably with regard to battery life, illumination, and field of view throughout the examination period. The specific tests and Given's equivalent test are described in greater detail below.

Special Control Objective	Existing Special Control for Endoscopes/ Enteroscopes	Suggested Analogous Special Control for Ingestible Telemetric Video Diagnostic Imaging Devices
Biocompatibility	ISO 10993 assay, as appropriate for the materials	ISO 10993 assays, as appropriate for the materials
Electrical Safety	IEC 60601-1-1 assessments	IEC 60601-1-1 assessments
Electromagnetic Compatibility	IEC 60601-1-2 assessments	IEC 60601-1-2 assessments
Electromagnetic Interference	IEC 60601-1-2 assessments	IEC 60601-1-2 assessments
RF Propagation	IEC 60601-1-2 assessments	IEC 60601-1-2 assessments and

Special Control Objective	Existing Special Control for Endoscopes/ Enteroscopes	Suggested Analogous Special Control for Ingestible Telemetric Video Diagnostic Imaging Devices
		compliance with applicable FCC regulations
Obscured Optical Pathway	Animal testing	Animal testing and human clinical studies
Video Unit Integrity	N/A	Compression force testing
Battery Life	N/A	Bench testing based on observed transit time in human clinical assessments
Illumination	N/A	Human clinical assessments
Field of View	N/A	Human clinical assessments

These tests allow manufacturers to assure the safety and effectiveness of ingestible telemetric video diagnostic imaging devices by demonstrating that: (1) the device is electrically safe and compatible with other medical devices and RF environments; (2) passes through gastrointestinal system without obscuring the optical images; and (3) captures images with adequate illumination for visualization throughout the passage period.

As additional specific special controls regarding: (1) interference caused by RF energy sources and potential data loss; (2) interference with video image device passage through the gastrointestinal system; and (3) medical review of the captured images, Given intends to label the device with the following caution and precaution statements.

1. Proposed Cautions

"Physicians should consider doing a small bowel series before utilizing the M2A® Capsule in patients who are suspected of suffering from fistulae or strictures.";

"In a small number of cases, the M2A® Capsule may not image the entire small bowel due to variation in patient GI motility." and;

"Final diagnosis based on the RAPID video should be made only by physicians who are trained in the interpretation of endoscopic images."

2. Proposed Precaution

"In the event that the patient is not able to avoid radio interference (e.g., from ham radio transmitter, MRI, etc.), some images may be lost, which occasionally may result in the physician having to repeat the capsule procedure. If such a case occurs and the capsule procedure has to be repeated, it would be advised for the patient to stay within the premises of the clinic to prevent this problem from recurring."

Given recommends that the labeling information and tests described above be established as special controls for ingestible telemetric video diagnostic imaging devices intended for the detection of pathologies as an adjunctive tool in the diagnosis of gastrointestinal disorders and diseases. Application of these controls to later 510(k) submissions will assure the safety and efficacy of these important ingestible telemetric video diagnostic imaging products.

VII. CLINICAL AND PRECLINICAL DATA

Given has not conducted any preclinical or clinical testing of the Given System that has not already been submitted to FDA in 510(k) notice K010312 or in response to questions during the review of the 510(k) notice.

VIII. SUBMITTER'S NAME AND ADDRESS

Gavriel Meron
President and CEO
Given Imaging Limited
Building 7, New Industrial Park
P.O. Box 258
Yoqneam 20692
Israel

IX. CONTACT PERSON AND TELEPHONE/FACSIMILE NUMBERS

Jonathan S. Kahan, Esq.
Hogan & Hartson, L.L.P.
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004-1109
Telephone: (202) 637-5794
Facsimile: (202) 637-5910

X. CONFIDENTIALITY

Given considers its intent to market the Given® Diagnostic Imaging System intended for the detection of pathologies as an adjunctive tool in the diagnosis of small bowel gastrointestinal disorders and diseases to be confidential commercial information.

In addition, some of the material in this application may be trade secret or confidential commercial or financial information within the meaning of 21 C.F.R. § 20.61 and therefore not disclosable under the Freedom of Information Act, even after the existence of the application becomes public knowledge. We ask that FDA consult with the company as provided in 21 C.F.R. § 20.45 before making any part of this submission publicly available.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUN 8 2001

Given® Imaging, Ltd.
c/o Mr. Jonathan Kahan
Hogan & Hartson, L.L.P.
Columbia Square
555 Thirteenth Street, N.W.
Washington, D.C. 20004-1109

Re: K010312
Given® Video System
Regulatory Class: III
Product Code: 78 NEZ
Dated: May 3, 2001
Received: May 4, 2001

Dear Mr. Kahan:

We have reviewed your Section 510(k) notification of intent to market the device referenced above. We have determined the device is not substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to any device which has been reclassified into class I (General Controls) or class II (Special Controls). This decision is based on the fact that your device (ingestible capsule) has a new indication of imaging the entire small bowel that alters the diagnostic effect, impacting safety and effectiveness, and is therefore a new intended use.

Therefore, this device is classified by statute into class III (Premarket Approval), under Section 513(f) of the Federal Food, Drug, and Cosmetic Act (Act).

Section 515(a)(2) of the Act requires a class III device to have an approved premarket approval application (PMA) before it can be legally marketed, unless the device is reclassified.

Any commercial distribution of this device prior to approval of a PMA, Product Development Protocol (PDP), or the effective date of any order by the Food and Drug Administration re-classifying this device into class I or II, would be a violation of the Act. Clinical investigations of this device must be conducted in accordance with the investigational device exemptions (IDE) regulations.

The Food and Drug Administration Modernization Act of 1997 (FDAMA), in section 207, deals with the Evaluation of Automatic Class III Designation. Under this section a manufacturer, whose device is found to be not substantially equivalent to a predicate device, can request FDA to make a risk-based classification for their device. I believe that based on the review of your device, it may be a candidate for Evaluation of Automatic Class III Designation. Therefore, you may wish to make such a request of this agency. For additional information on your options under Section 207, please refer to our guidance entitled, "New Section 513(f)(2) - Evaluation of Automatic Class III Designation, Guidance for Industry and Staff." This document is available on the World Wide Web/CDRH Home Page at: http://www.fda.gov/cdrh/modact/classiii.html.

If you wish to pursue the marketing of this device and need information or assistance for preparing investigational or premarket submissions, please contact the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or (301) 443-6597, or at its internet address "http://www.fda.gov/cdrh/dsmamain.html".

Sincerely yours,

Nancy C. Brogdon

Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health