BTG latest FDA inspections experience

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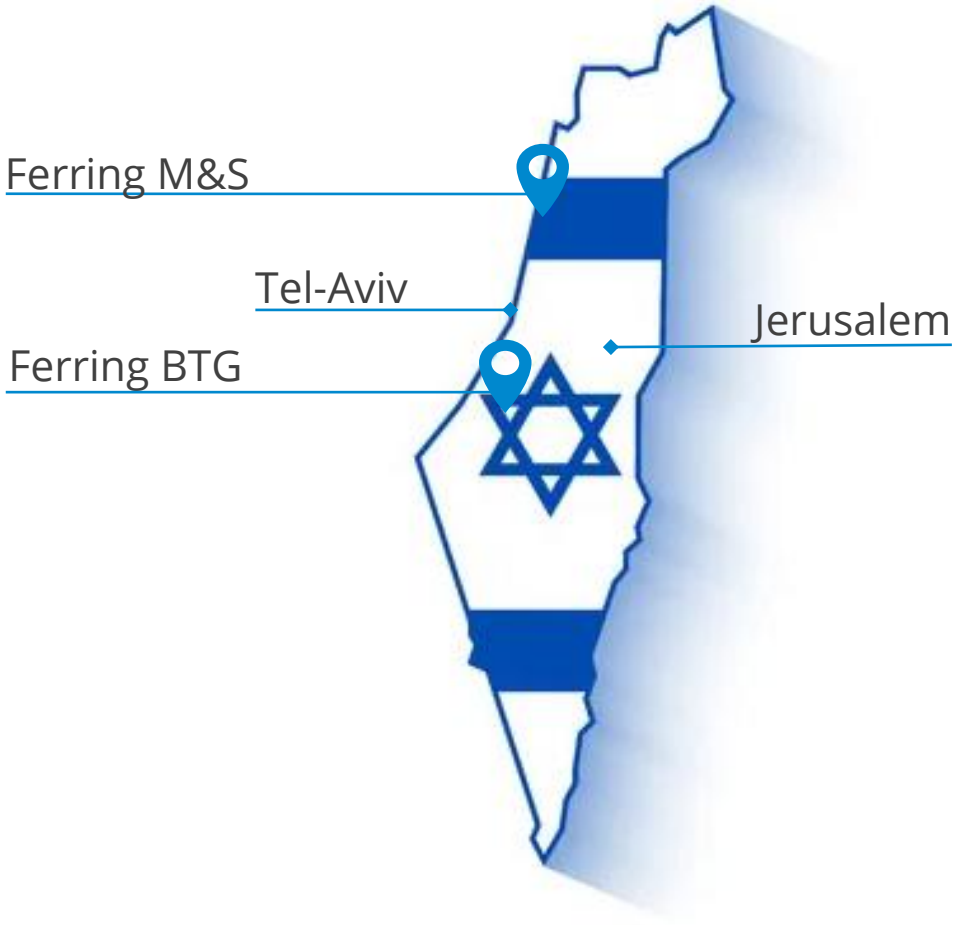
Presentation Contents

- Introduction
- FDA inspections recently held in BTG
- Preparations and challenges
- Inspection conductance
- Conclusions from late FDA view and BTG's experience

Company Introduction

- Founded in 1980 as a wholly-owned subsidiary of Bio-Technology General Corp.
- In July 2005, BTG was acquired by Ferring
- ~335 employees



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A FERRING COMPANY

BTG – A Ferring Company

Ferring Manufacturing Network

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Recombinant Drug Substances

Recombinant human Growth Hormone (Somatropin) DS

(NDA approved by FDA in 1995)

Pegloticase (Recombinant PEGylated Uricase) DS

(BLA approved by FDA in 2010)

Recombinant Follicular Stimulating Hormone (FSH) DS

(BLA submitted to FDA in August 2022; Subject of this PLI)

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Sodium Hyaluronate (NaHA) and its finished products (Medical Devices Class 3 under PMA) – EUFLEXXA and BIOLON Family of Products

Bulk NaHA

EUFLEXXA (approved by FDA in 2004)

BIOLON (approved by FDA in 1998)

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Two FDA inspections took place in BTG during Q1/2023

Dates - 23-26/01/2023

Products and scope –

periodic GMP inspection on BTG's medical devices marketed in the US

One inspector – USFDA Office of Regulatory Affairs (ORA),
conducts inspections in the area of Medical Devices & Rad Health.

Dates - 08-16/03/2023

Products and scope –

PLI (pre-licensing) inspection on Ferring's fertility product Rekovelle, recently submitted in the US

Four inspectors –

- Lead Auditor, Senior Pharmaceutical Assessor, Division of Biotechnology Manufacturing
- Consumer Safety Officer, ORA
- Two Biologists, Division of Biotechnology Review & Research

Main Challenges in Management of the first Inspection

- Prior to the inspection, the FDA investigator did not provide any agenda, requests for documents or lists of quality records.
- The FDA investigator stated in the beginning of the inspection that the inspection hours will not be identical to the site working hours; indeed, during most inspection days, the inspection was completed in late hours
- It seems that the FDA investigator was not familiar with BTG activities related to the medical devices marketed in the US
- During the inspection, the FDA investigator requested to provide her with English translations of several BTG's documents that are written in Hebrew; She requested the translations within ~12 hours
- Most of the inspection time was focused on document review; compared to other inspections, less time was devoted to on-site tours

Main Challenges in Management of the second Inspection

- Prior to the inspection, the FDA investigators did not provide any agenda
- A huge number of documents and records were requested about a week before the audit
- PLI audit purpose is to inspect both readiness for commercial manufacturing and conformance to application
- Most of the time, the inspection was conducted in 3-4 separate channels, while SMEs are skipping from one inspector to the other
- The inspection included both on-site tours and document review; often more than one tour and document review in parallel

What went well (1)

The preparations to the inspections were proven to be effective and relevant, including:

Reviewing of the investigators published 483

Preparation in advance of presentations presenting important topics and areas

Preparation and practicing with the SMEs that presented the topics to the investigators

Documents that are “always requested” were prepared in advance, in order to save time during the audt

What Went Well

- Strong and professional back room: documents, information and answers were supplied to the FDA investigators promptly and efficiently
- BTG is taking a proactive approach during the inspections, at the end of each inspection day, the QA team had reviewed all comments/discussions/potential observations/requests, prepared answers and presented to the FDA investigators at the next audit date, to assure that there are no open issues or topics that need to be clarified
- At the end of each day, a summary of the inspection day was prepared and sent to all BTG employees; this enhanced the engagement, awareness and readiness of all employees

Pink sheet assumption

FDA challenge - how to catch up on inspections after the COVID-19 travel disruptions of the past three years.

FDA may use record reviews to fulfill the statutory requirements for periodic inspections

The law also explicitly allows the FDA to rely on foreign regulatory partners in the context of pre-approval inspection, not just for surveillance inspections

תודה על ההקשבה