DISCOVER

Assembly, Label & Pack

Tucked away in a space just outside of Cambridge that's just 800 square feet — no larger than an average two-bedroom apartment — resides a talented team of just five people who assemble, label and pack 65 percent of Biogen Idec's materials for clinical use worldwide.

Across the ocean, an equally dedicated team of 50 employees in Hillerød, Denmark assembles, labels and packs all of the company's products for commercial use — a staggering array of 145 different presentations sold in more than 90 markets globally.

Together, they represent less than one percent of Biogen Idec's workforce, but they fulfill virtually all of the company's needs for assembling, labeling and packing its disposable, plastic drug-delivery systems.

FAST FACT

The Cambridge team supports clinical trials and the Hillerød team assembles, labels and packs products for commercial use

FAST FACT

Cambridge now supports 60 to 70 clinical protocols worldwide. This number will increase to 300 protocols by 2016, without adding any additional operators

Capabilities

The remarkable output of these two teams originates from their flexible, nimble approach to preparing materials for patient use. A brand new production line can be installed within three months to accommodate a product launch or the start of a new clinical trial. As market demands shift, the teams can quickly adjust their volumes up or down using either manual, semi-automatic or automatic production lines to accommodate each respective need.

Housing this function within the company allows a greater degree of control and customization at a lower cost than outsourcing would allow. For example, the Cambridge team offers vial or package inserts in 40 different languages to accommodate a wide range of markets.

What's New

Patient convenience and ease of use are paramount, and continuous product upgrades reflect this emphasis. The most recent example is the AVONEX Pen, which is now being modified from a seven-step injection device to just two – removal of the cap and injection into the leg.

Increased demand for products is also driving growth at the Cambridge facility, which will expand from 800 feet to 3,200 square feet by 2016. The new capacity will triple the output without adding any additional operators.

FAST FACT

Cambridge is scheduled to produce more than 14,000 clinical kits and label nearly 500,000 components in 2014

Commercial Products Assembled, Labeled and Packed In Hillerød

AVONEX (interferon beta-1a)

AVONEX PEN (interferon beta-1a)

plegridy (peginterferon beta-1a)

TYSABRI (natalizumab)

ALPROLIX [Coagulation Factor IX (Recombinant), Fc Fusion Protein]

ELOCTATE [Antihemophilic Factor (Recombinant), Fc Fusion Protein]

FAST FACT

Hillerød is scheduled to package more than 1.4 million units in 2014 – an output increase of more than 100 percent since 2009

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The Oral Solid Dose Facility

This best-in-class facility in Research Triangle Park is a small, but robust, hub of activity within the Global Manufacturing organization. It serves as a prime example of Biogen Idec's relentless commitment to meet patient demand through continuous investment in manufacturing infrastructure.

Facility Overview

The Oral Solid Dose (OSD) facility is the only Biogen Idec site that manufactures small molecule therapies – synthetically produced medicine delivered in the form of capsules and tablets. TECFIDERA, Biogen Idec's premier small molecule therapy, is the leading oral treatment for relapsing MS. The OSD facility began manufacturing TECFIDERA in 2014 after retrofitting the Eisai plant with new equipment and partnering with Eisai to share manufacturing space.

FAST FACT

4.4 million TECFIDERA microtablets are produced per hour by the tablet press at the OSD facility

TECFIDERA production is currently in full swing at the OSD site as the new equipment is validated in preparation for FDA licensure – anticipated in the spring of 2015. Until licensure occurs, patients will receive TECFIDERA produced by contract manufacturers in Europe.

The talented team of more than 90 employees at the OSD facility also apply their vast knowledge and expertise to the production of Eisai medicines, serving as contract manufacturers for several small molecule therapies, including:

- Lunesta for insomnia (market: Japan)
- Banzel for epilepsy (markets: U.S. and Canada)
- Aciphex for acid reflux (market: U.S.)
- Aricept for Alzheimer's disease (market: U.S.)

Biogen Idec and Eisai employees have formed a true partnership – sharing resources, facilities and communal lunch rooms – to make this unique and innovative manufacturing enterprise a model for success.

FAST FACT

Biogen Idec and Eisai employees share the same facility, thereby enhancing the level of partnership and cooperation

Facility Capabilities

Step inside this small molecule manufacturing facility and you will see granulators, blenders and machines for compression and encapsulation – all the ingredients and equipment used to make millions of tablets and capsules.

The OSD manufacturing process involves several critical activities to ensure a quality tablet or capsule, such as precise measuring and weighing of dry ingredients; wetting them for proper adhesion; milling and blending the mixture, compressing it into the proper shape; applying a protective coating to the tablets; and placing the appropriate quantity of tablets into a capsule.

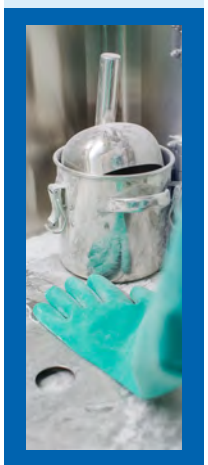
Small molecule production also requires world-class analytics and quality assurance to ensure the therapies have the proper chemical and physical characteristics to survive the production process while retaining optimal purity and efficacy.

FAST FACT

A batch of TECFIDERA treats 1,096 MS patients each year and the average cycle time for a batch is 35 days – best-in-class

The following seven steps ensure the purity, safety and efficacy of each and every pill produced at the OSD facility:

Dispensing – involves prepping and weighing the active and inactive ingredients that make up the tablets and capsules.

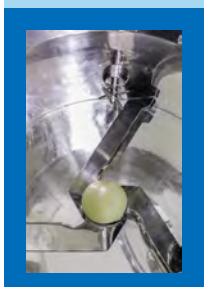


1

Blending and Milling – ensures consistency of the active ingredients. Milling grinds the particles to achieve the desired size while blending combines these particles to form a homogenous mixture.

2

Wet Granulation – uses water or solvent-based solutions to create a consistent particle size and blend by placing the raw materials in a bowl, mixing them and wetting them with a solution.



3

Fluid Bed Drying of Granulation – moves warm air through the wet granulation to remove the water or solvent to ensure the blend is ready for the next step.

4

Tablet Compression – tablets begin to take shape during this step, which involves feeding the blend into a press, applying pressure to form the tablets, and de-dusting them to remove excess powder.

5

Tablet Coating – sprays a solution onto the tablets to enhance their flavor, appearance and efficacy; and to promote optimal absorption and to prevent stomach irritation.

6

Encapsulation – places certain formulations into capsule shells made of gelatin or similar digestible materials to ensure they are firm enough to hold the ingredients and maintain their stability.

7

FAST FACT

The OSD facility has produced 150-plus batches with a very high success rate – 97 percent of product manufactured will be suitable for release to the market

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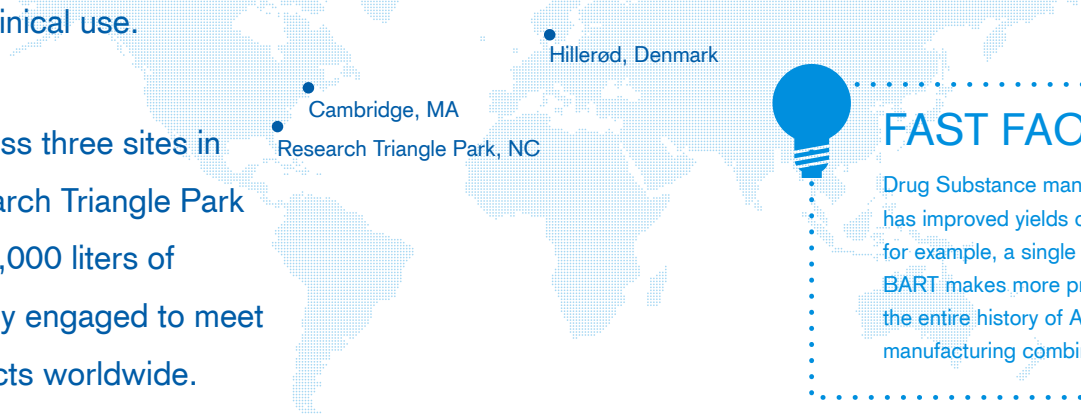
Drug Substance Manufacturing

A truly global enterprise, Biogen Idec's Drug Substance manufacturing operation supplies medicines to patients in more than 30 countries worldwide. Patients with a variety of conditions benefit from the company's massive capacity to cultivate and grow cells in state-of-the-art bioreactors that produce nearly two dozen Biogen Idec products for commercial and clinical use.

More than 850 employees across three sites in Cambridge, Hillerød and Research Triangle Park ensure that the company's 198,000 liters of bioreactor capacity are optimally engaged to meet the varying demands for products worldwide.



FAST FACT

Drug Substance manufacturing has improved yields over time — for example, a single batch of BART makes more product than the entire history of AVONEX manufacturing combined

FAST FACT

Drug Substance capacity has increased exponentially: In 2003, the team produced two commercial products. Today, five commercial products are produced along with many more clinical programs

Facilities Overview

Cambridge

231 Employees

Five 2,000-liter production bioreactors

Commercial products manufactured:
- AVONEX
- PLEDGRIDY
- ELOCTATE
- ZEVILIN

Clinical pipeline products:
- LINGO
- BART
- NEUBLASTIN
- TWEAK

Hillerød

280 Employees

Six production bioreactors with 15,000 liters of capacity each

Commercial products
- TYSABRI
- Three biosimilars
- One product for an outsourcing partner

Clinical pipeline products:
- LINGO

Research Triangle Park

338 Employees

Eleven production bioreactors with capacity ranging from 1,000 – 15,000 liters

Products manufactured:
- Commercial: TYSABRI, ALPROLIX, AVONEX, PLEGRIDY, ELOCTATE
- Mid-stage pipeline: LINGO, BART, NEUBLASTIN, TWEAK, STX-100, ZINBRITA
- Early-stage pipeline: STX-200, CD40, aBDCA2, ALPHA SYNUCLEIN,OSMR
- Two biosimilar products
- Twelve products for outsourcing partners

Process Overview

The following steps ensure the purity, safety and efficacy of each and every batch produced. Production time for one large-scale batch is 55 to 60 days.

1 Cell Banking
This is only performed at the Cambridge facility. Working cell bank vials are sent to all of the Drug Substance sites and stored in a liquid nitrogen freezer until needed for manufacturing.

2 Inoculum Expansion
Cell bank vials are thawed in flasks to start the process. Cells are expanded to increase their numbers and density in preparation for the next phase. This process takes several days.

3 Cell Production
Cells are further expanded in stainless steel bioreactors, referred to as the seed train. As they multiply, cells are transferred to larger bioreactors to maintain a consistent amount of cells per volume. The process is monitored closely with many probes and sensors as cells move through bioreactors of increasing size to expand the number and density of cells. Nutrients are supplied to the culture in which the cells grow.

4 Product Harvest
At the completion of bioreactor scale up, the product is harvested using filtration or centrifugation methods.

5 Purify & Viral Filtration
Chromatography is performed to isolate the target protein from major impurities. The type and number of chromatography columns used varies depending on the product and its properties. Viral filtration removes potential viral contaminants from the product.

6 Ultrafiltration
Usually performed near the end of the purification process to both concentrate the product and to exchange the buffer of the bulk drug substance.

7 Bottling / Bagging
Bulk drug substance is filled into bottle or bags, depending on product requirements. Individual container volumes vary from two to 50 liters.

FAST FACT

There are 220 trillion cells in a 15,000-liter batch of TYSABRI

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