PEMBROLIZUMAB

PROCESS DEVELOPMENT IN PERSISGEN PAR:

Pembrolizumab (MK-3475) is a humanized monoclonal antibody that is expressed as a secreted product from a suspension Chinese Hamster Ovary (CHO) cell line.

A fully characterized Master Cell Bank (MCB) as well as a Working Cell Bank (WCB) was established. Cells from the WCB are expanded in shake flasks to generate the inoculum for a production bioreactor to produce the antibody product. The downstream processing includes chromatography, viral clearance, ultrafiltration/ diafiltration, and a final 0.2 μm filtration steps.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D and industrial scale was the production in 5 and 50 liter bioreactor, respectively. The protein expression was up to 3 gr/L and purification productivity was up to 75%.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Antineoplastic
IgG4 isotype antibody
PD-1/PD-L1 Inhibitor
Mechanism of action:
A humanized monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2. The PD-1 receptor found on T cells and PD-L1 and PD-L2 ligands have been found to be abnormally expressed by tumor cells, this interaction cause to release PD-1 pathway-mediated that inhibits T cell proliferation, cytokine production and the immune response, including the anti-tumor immune response.
Indications:
Melanoma, NSCLC, HNSCC, cHL (adult and pediatric), PMBCL (adult and pediatric), urothelial carcinoma, MSI-H/dMMR cancers (adult and pediatric), gastric cancer, cervical cancer, HCC, MCC (adult and pediatric) and RCC

ORIGINAL PRODUCT INFORMATION

Keytruda
MERCK SHARP & DOHME LIMITED
US patent year: 2014
Price and Average Annual Sales:
About ($2,000 to $4,000)/vial and $9 billion/year
Dosage Forms & Strengths:
injection, lyophilized powder for reconstitution

- 50mg/vial

injectable solution

- 100mg/4mL (25mg/mL)

Storage condition:
Refrigeration between 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 15 months.
Startup company: Tahagen.
Project stage: The technology is transferred to CinnaGen Co.

VEDOLIZUMAB

PROCESS DEVELOPMENT IN PERSISGEN PAR:

The humanized IgG1 monoclonal antibody, vedolizumab, is produced in Chinese hamster ovary (CHO) cells which are engineered using recombinant DNA technologies. After cell culture production, vedolizumab is purified from supernatant using standard chromatographic and filtration techniques, then the purified antibody is brought to the target concentration. Vedolizumab is sterile filtered into vials and lyophilized prior to final packaging.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D and industrial scale was the production in 5 and 50 liter bioreactor, respectively. The protein expression was up to 3 gr/L and purification productivity was up to 75%.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Anti-inflammatory
IgG1 isotype antibody
Human lymphocyte α4β7 integrin blocker
Mechanism of action:
A humanized Monoclonal Antibody that works as antagonist to α4β7 integrin. The drug binds to α4β7 integrin, a mediator of gastrointestinal inflammation and decreases inflammation in the gastrointestinal tract by blocking the entry of inflammation-stimulating lymphocytes.
Indications:
Ulcerative Colitis (adult), Crohn Disease (adult), Graft vs. Host Disease

ORIGINAL PRODUCT INFORMATION

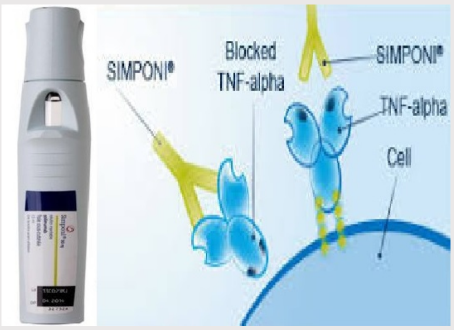
Entyvio
Takeda Pharmaceutical Company
US patent year: 2012
Price and Average Annual Sales:
About ($5,000 to $6,000)/vial and $2.5 billion/year
Dosage Forms & Strengths:
injection, lyophilized powder for reconstitution

- 300mg/vial

Storage condition:
Refrigeration between 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 14 months.
Startup company: Radin Zist Fanavar.
Project stage: The technology is transferred to AryoGen Pharmed Co.



PROCESS DEVELOPMENT IN PERSISGEN PAR:

The humanized IgG1 monoclonal antibody, Golimumab, is produced in murine myeloma cell lines (SP2/0) which are engineered using recombinant DNA technologies.
The drug substance producing process contains cell culture stages including cell culture in flasks for inoculation of the bioreactor and bioreactor culture and purification stages. The purification of the cell culture harvest includes a series of chromatography, ultra-diafiltration and viral inactivation and filtration steps.
Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well.
The R&D scale was the production in 5 liter bioreactor. The protein expression was up to 600 mg/L and purification productivity was up to 75%.
Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

GOLIMUMAB

ACTIVE SUBSTANCE INFORMATION

Description:
Anti-inflammatory (immunosuppressive)
IgG1 isotype antibody
Tumor necrosis factor alpha (TNF-α) inhibitor
Mechanism of action:
A humanized monoclonal antibody that inhibits human TNFα (both soluble and transmembrane) from binding to its receptors. The drug is an effective modulator of inflammatory markers that targets and neutralizes excess TNF-alpha protein, which cause to decrease in C-reactive protein (CRP) levels, interleukin (IL)-6, intercellular adhesion molecules (ICAM)-1, matrix metalloproteinase (MMP)-3, and vascular endothelial growth factor (VEGF).
Indications:
Rheumatoid arthritis, Psoriatic arthritis, Ankylosing spondylitis, and Ulcerative colitis

ORIGINAL PRODUCT INFORMATION

Simponi
Janssen Biotech, Inc.
US patent year: 2009
Price and Average Annual Sales:
About ($5,000 to $6,000)/dose and $2 billion/year
Dosage Forms & Strengths:
prefilled autoinjector:
- 50 mg/0.5 mL and 100 mg/1 mL

single-dose prefilled syringe:
- 50 mg/0.5 mL and 100 mg/1 mL

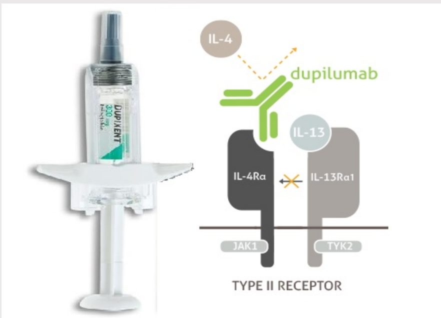
injectable solution:
- 50 mg/4mL (Simponi Aria vial)

Storage condition:
Refrigeration between 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 13 months.
Startup company: Arnagen Pharmed.
Project stage: The technology is ready for transfer.

DUPILUMAB



PROCESS DEVELOPMENT IN PERSISGEN PAR:

Dupilumab is a recombinant, fully human IgG4 monoclonal antibody against interleukin (IL)-4 receptor alpha that inhibits IL-4/IL-13 signaling and cytokine-induced inflammatory responses.
The drug substance produced in a Chinese hamster ovary (CHO) cell line by recombinant DNA technology. Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale bioreactors, respectively, and purification stages including the clarification of harvest, a series of chromatography and polishing, viral inactivation and ultra-diafiltration/ filtration steps.
Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well.
The R&D scale was the production in 5 liter bioreactor. The protein expression was up to 3 gr/L and purification productivity was up to 75%.
Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description
Anti-inflammatory
IgG4 isotype antibody
An interleukin-4 receptor alpha antagonist
Mechanism of action:
A humanized monoclonal antibody that binds to the alpha subunit of the interleukin-4 receptor (IL-4Rα), making it a receptor antagonist. Through blockade of IL-4Rα, the drug modulates signaling of both the interleukin 4 and interleukin 13 pathways. Inflammatory processes associated with type 2 helper T-cell (Th2) immunity that the activation of Th2 cells is characterized by the production of interleukin (IL) 4, IL-5, IL-9, and IL-13. Th2-associated cytokines, such as IL-4 and IL-13, play a central role in the pathophysiology of the inflammatory conditions such as asthma and atopic diseases.
Indications
Moderate-to-severe atopic dermatitis such as eczema, Asthma

ORIGINAL PRODUCT INFORMATION

Dupixent
Sanofi-Aventis, Inc.
US patent year: 2013
Price and Average Annual Sales:
About ($1,500 to $3,200)/dose and $4 billion/year
Dosage Forms & Strengths

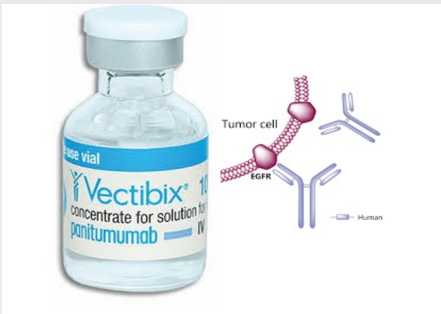
- Single-dose pre-filled syringe: 300 mg/2 mL
- Single-dose pre-filled syringe: 200 mg/1.14 mL

Storage condition
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 15 months.
Startup company: Zist Pharmed Iranian.
Project stage: The technology is ready for transfer.

PANITUMUMAB



PROCESS DEVELOPMENT IN PERSISGEN PAR:

Panitumumab is a recombinant, fully human IgG2 monoclonal antibody that binds with high affinity and specificity to the ligand binding domain of EGFR and inhibits receptor autophosphorylation induced by all known EGFR ligands. Binding to EGFR results in internalisation of the receptor, inhibition of cell growth and induction of apoptosis.

The drug substance produced in a mammalian cell line (CHO) by recombinant DNA technology. Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale bioreactors, respectively, and purification stages including the clarification of harvest, a series of chromatography and polishing, viral inactivation and ultra-diafiltration/ filtration steps.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D scale was the production in 5 liter bioreactor. The protein expression was up to 2.5 gr/L and purification productivity was up to 70%.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Antineoplastic agents
IgG2 isotype antibody
Binds to the human epidermal growth factor receptor (EGFR)
Mechanism of action:
A humanized monoclonal antibody that binds specifically to EGFR on both normal and tumor cells, and competitively inhibits the binding of ligands for EGFR. The intracellular processes triggered by activation of EGFR (dimerization, autophosphorylation and signal transduction) are prevented by the drug, leading ultimately to increased apoptosis, reduced proliferation of tumour cells and reduced angiogenesis. Tumour growth and development of metastases are prevented.
Indications:
(EGFR)-expressing, metastatic colorectal carcinoma (mCRC) with disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.

ORIGINAL PRODUCT INFORMATION

Vectibix
Amgen, Inc.
US patent year: 2006
Price and Average Annual Sales:
About ($1,300 to $5,200)/dose and $2 billion/year
Dosage Forms & Strengths

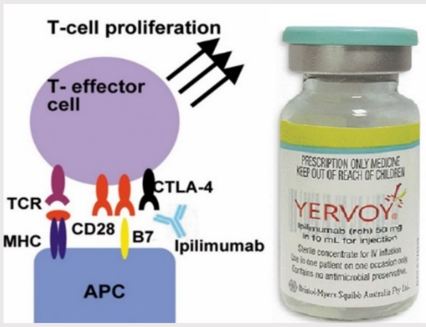
- Single-use vials (20 mg/mL):
  100 mg/5 mL, 200 mg/10 mL, 400 mg/20 mL

Storage condition
Refrigeration at 2- 8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 14 months.
Startup company: Arnagen Pharmed.
Project stage: The technology is ready for transfer.

IPILIMUMAB



PROCESS DEVELOPMENT IN PERSISGEN PAR:

Ipilimimab is a recombinant, fully human IgG1 monoclonal antibody and CTLA-4 immune checkpoint inhibitor that blocks T-cell inhibitory signals induced by the CTLA-4 pathway, increasing the number of reactive T-effector cells which mobilize to mount a direct T-cell immune attack against tumor cells.

The drug substance produced in a Chinese hamster ovary (CHO) cell line by recombinant DNA technology. Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale bioreactors, respectively, and purification stages including the clarification of harvest, a series of chromatography and polishing, viral inactivation and ultra-diafiltration/ filtration steps.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D scale was the production in 5 liter bioreactor, the protein expression was up to 2.5gr/L and purification productivity was up to 75%.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Antineoplastic agents
IgG1 isotype antibody
A Cytotoxic T-lymphocyte antigen-4 (CTLA-4) immune checkpoint inhibitor
Mechanism of action:
A humanized monoclonal antibody that produces an exacerbated autoimmunity. The CTLA-4 is a cell surface molecule that plays an essential role in regulating the adaptive immune response. After T-cell activation, CTLA-4 will be upregulated and it will compete on the binding between CD28 and B7. The binding between CTLA-4 and B7 interrupts the stimulatory signal which in order blunts T-cell proliferation response. The drug is designed to block the activity of CTLA-4, thereby sustaining a potent T-cell response against tumor cells.
Indications:
Melanoma, Renal Cell Carcinoma (RCC)

ORIGINAL PRODUCT INFORMATION

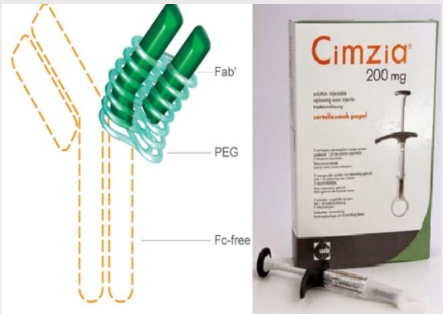
Yervoy
Bristol-Myers Squibb Pharma EEIG, Inc.
US patent year: 2011
Price and Average Annual Sales:
About ($7,800 to $30,900)/dose and $2 billion/year
Dosage Forms & Strengths:

- Single-use vials (5 mg/mL):
  50 mg/10mL, 200 mg/40 mL

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 14 months.
Startup company: Rastakgen.
Project stage: The technology is ready for transfer.



CERTOLIZUMAB PEGOL

PROCESS DEVELOPMENT IN PERSISGEN PAR:

Certolizumab pegol is a recombinant, humanized antibody Fab' fragment against tumor necrosis factor alpha (TNFα).

The drug substance produced in Escherichia coli by recombinant DNA technology using fed-batch fermentation process and conjugated to polyethylene glycol (PEG). Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale fermentors, respectively, and purification stages including the clarification of harvest, a series of chromatography and polishing steps, viral inactivation and ultra-diafiltration/ filtration steps.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well.

The R&D scale was the production in 5 liter fermentor with up to 4gr/L protein expression.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Immunosuppressant
Antibody Fab' fragment
A tumor necrosis factor (TNF) blocker
Mechanism of action:
A humanized antibody Fab' fragment that conjugated to polyethylene glycol and binds to soluble and membrane-bound TNF-α, inhibiting the pro-inflammatory actions of this cytokine. Attachment of polyethylene glycol to Fab and the elimination of the constant fragment of immunoglobulin (Fc), without inducing complement or antibody-dependent cytotoxicity, increases its plasma half-life.
Indications:
Reducing signs and symptoms of Crohn’s disease
Moderately to severely active rheumatoid arthritis
Active psoriatic arthritis
Active ankylosing spondylitis

ORIGINAL PRODUCT INFORMATION

Cimzia
UCB Pharma S.A., Inc.
US patent year: 2008
Price and Average Annual Sales:
About $4,600/dose and $1.8 billion/year
Dosage Forms & Strengths:

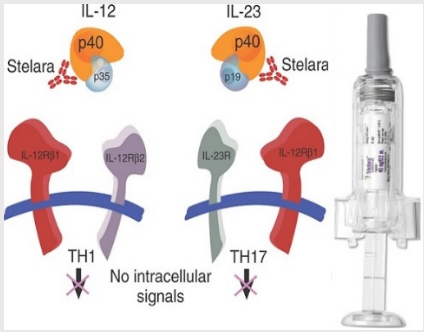
- Single-use pre-filled syringe: 200 mg/mL
- Single-use vial: 200 mg Lyophilized powder with 1mL of sterile Water

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 12 months.
Startup company: Arnagen Pharmed.
Project stage: Technology is ready for transfer.

USTEKINUMAB



PROCESS DEVELOPMENT IN PERSISGEN PAR:

Ustekinumab is a recombinant, fully human IgG1 monoclonal antibody that binds with specificity to the shared p40 protein subunit of human cytokines interleukin (IL)-12 and IL-23 and by preventing p40 from binding to the IL-12Rβ1 receptor protein expressed on the surface of immune cells, inhibits the bioactivity of IL-12 and IL-23.
The drug substance produced in a Sp2/0 murine myeloma cell line by recombinant DNA technology. Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale bioreactors, respectively, and purification stages including the clarification of harvest, a series of chromatography and polishing steps, viral inactivation and ultra-diafiltration/ filtration steps. Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D and industrial scale was the production in 5 and 50 liter bioreactor, respectively. The protein expression was up to 600 mg/L and purification productivity was up to 70%.
Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Immunosuppressants
IgG1 isotype antibody
A human interleukin-12 and -23 antagonist
Mechanism of action:
A humanized monoclonal antibody that blocks interleukin IL-12 and IL-23 by binding with high affinity and specificity to the p40 subunit of IL-12 and IL-23, which help activate certain T-cells, therefore disrupting the pro-inflammatory pathway that contributes to several chronic diseases.
Indications:
Moderate to severe plaque psoriasis (Ps)
Active psoriatic arthritis (PsA)
Moderately to severely active Crohn's disease (CD)

ORIGINAL PRODUCT INFORMATION

Stelara
Janssen-Cilag International NV, Inc.
US patent year: 2009
Price and Average Annual Sales:
About ($1,700 to $23,000)/dose and $5.2 billion/year
Dosage Forms & Strengths:

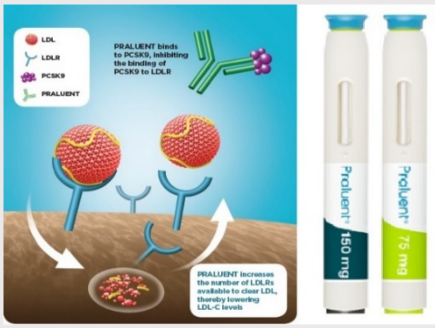
- Single-use pre-filled syringe: 45 mg/0.5 mL
- Single-use pre-filled syringe: 90 mg/mL
- Single-use vials (5 mg/mL): 130 mg/26 mL

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 18 months.
Startup company: Arses Zist Darou.
Project stage: Technology is transferred to Saman Daroo 8.

ALIROCUMAB



PROCESS DEVELOPMENT IN PERSISGEN PAR:

Alirocumab is a recombinant, fully human IgG1 monoclonal antibody that binds with high affinity and specificity to proprotein convertase subtilisin kexin type 9 (PCSK9). PCSK9 binds to the low-density lipoprotein receptors (LDLR) on the surface of hepatocytes to promote LDLR degradation within the liver.
The drug substance produced in a Chinese hamster ovary (CHO) cell line by recombinant DNA technology. Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale bioreactors, respectively, and purification stages including the clarification of harvest, a series of chromatography and polishing steps, viral inactivation and ultra-diafiltration/ filtration steps.
Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well.
The R&D scale was the production in 5 liter bioreactor. The protein expression was up to 1.5 gr/L and purification productivity was up to 70%.
CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Lipid modifying agents
IgG1 isotype antibody
Binds to proprotein convertase subtilisin kexin type 9 (PCSK9)
Mechanism of action:
A humanized monoclonal antibody and a new class of cholesterol-lowering medications that inactivate a protein in the liver called PCSK9. PCSK9 typically binds to the LDL receptors (LDLR) in serum and marks them for lysosomal degradation and less LDL cholesterol being removed from circulation. Inhibiting PCSK9 prevents the LDLR from being degraded, and promotes removal of LDL cholesterol from circulation.
Indications:
primary hypercholesterolemia (heterozygous familial and non-familial) or mixed dyslipidemia

ORIGINAL PRODUCT INFORMATION

Praluent
Sanofi-Aventis, Inc.
US patent year: 2009
Price and Average Annual Sales:
About $5,850/patient in year and $307 million/year
Dosage Forms & Strengths:

- Single-use pre-filled pen: 75 mg/mL
- Single-use pre-filled pen: 150 mg/mL
- Single-use pre-filled syringe: 75 mg/mL
- Single-use pre-filled syringe: 150 mg/mL

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 14 months.
Startup company: Atingen Rad.
Project stage: The technology is ready for transfer.

ANAKINRA

PROCESS DEVELOPMENT IN PERSISGEN PAR:

Anakinra, the active substance, is a recombinant form of human interleukin-1 receptor antagonist (r-metHu IL-1ra).

The drug substance is produced by E. coli. Fermentation which is comprised of cell expansion of the master cell bank, inoculation of the fermentor, cell growth in the fermentor, induction of product and cell harvest. Afterwards, the cells are lysed, and the lysate is collected for further processing. Purification of Anakinra is accomplished by a sequence of clarification, chromatographic and filtration steps for the generation of filtered purified bulk product.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D and industrial scale was the production in 5 and 50 liter fermentor, respectively that the final yield is 500 mg/L of media culture.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Anti-inflammatory
Recombinant nonglycosylated protein
Interleukin-1 receptor antagonist (IL-1Ra)
Mechanism of action:
A recombinant form of human IL-1Ra that competitively inhibits binding of IL-1α and IL-1β to the IL-1 receptor type and blocks signal transduction. On the genetic and molecular basis of the auto-inflammatory syndromes, IL-1β plays a key role in inflammation, and the successful intervention with Anakinra in these syndromes provides the best evidence for such a role of IL-1.
Indications:
Rheumatoid arthritis, neonatal-onset multisystem inflammatory disease (NOMID).

ORIGINAL PRODUCT INFORMATION

Kineret
Amgen Inc.
US patent year: 2001
Price and Average Annual Sales:
About $155/dose and $165 million/year
Dosage Forms & Strengths:
single-dose prefilled syringe:

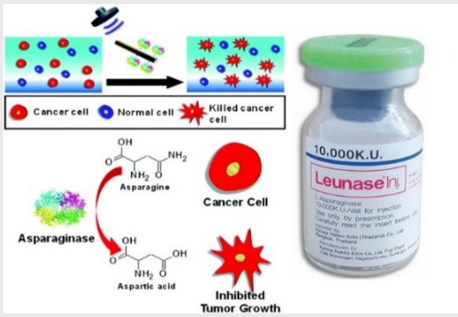
- 100 mg/0.67 mL (150 mg/mL)

Storage condition:
Refrigeration between 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 13 months.
Owner: PersisGen Par.
Project stage: Technology is being Scaled up to industrial phase in PersisGen Par CDMO facility.

L-ASPARAGINASE



PROCESS DEVELOPMENT IN PERSISGEN PAR:

This active substance, L-Asparginase, is a recombinant enzyme that is responsible for the metabolism of L-asparagine, by catalyzing L-asparagine into L-aspartic acid and ammonia.
L-Asparginase is produced in E. coli cells by a fermentation process that is comprised of cell expansion of the master cell bank, inoculation of the fermentor, cell growth in the fermentor, induction of product, and cell harvest. Afterwards, the cells are lysed, and the lysate is collected for further processing. Purification of L-Asparginase is accomplished by a sequence of clarification, chromatographic and filtration steps.
Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D and industrial scale was the production in 5 and 50 liter fermentor, respectively with 700 mg/L final yield.
Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Antineoplastic
Depletion of asparagine and protein synthesis inhibition of leukemic blasts
Mechanism of action:
An enzyme that catalyzes the hydrolysis of l-asparagine to l-aspartic acid and ammonia. Asparagine is a non-essential amino acid that maintains DNA, RNA and protein synthesis and promotes cell growth. Acute lymphoblastic leukemia cells and some other suspected tumor cells are unable to synthesize the non-essential amino acid asparagine, whereas normal cells are able to make their own asparagine, thus leukemic cells require high amount of asparagine. The drug deplete plasma levels of asparagine in leukemic cells by converting L-asparagine, leading to inhibition of cell growth; and ultimately the activation of apoptotic cell-death mechanisms.
Indications:
acute lymphoblastic leukemia, acute myeloid leukemia, non-Hodgkin's lymphoma

ORIGINAL PRODUCT INFORMATION

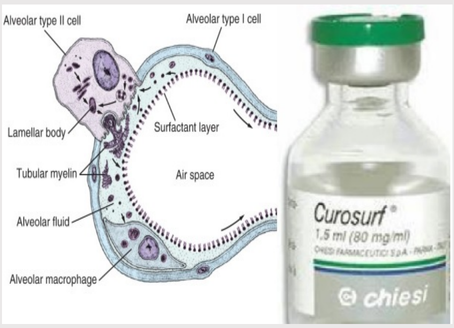
Leunase
Kyowa Hakko Kirin Co., Ltd.
US patent year: 1982
Price and Average Annual Sales:
About ($20 t0 $30)/dose, $380 million/year and $420 million/year in 2025
Dosage Forms & Strengths:
injection, lyophilized powder for reconstitution:

- 5000K.U. and 10000K.U. (per vial)

Storage condition:
Refrigeration between 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 10 months.
Startup company: Nano Darou Pajouhan.
Project stage: Technology is being Scaled up to industrial phase for the production of drug substance in PersisGen Par CDMO facility and drug product by Nano Darou Pajouhan.



PROCESS DEVELOPMENT IN PERSISGEN PAR:

Sheep lung surfactant extraction and purification process involves several steps including mammalian lung tissue fragmentation and mincing, the crude lung aqueous extract preparation, precipitation and separation of the pulmonary surfactant compounds, organic extraction of pulmonary surfactant sediment, depletion of solvents and other impurities, clarification and sterilization of the formulated pulmonary surfactant.
Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well.
The R&D and industrial scale was the product extraction from 1 and 100 kilogram of tissue, respectively with 300 mg/lung final yield.
Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

SHEEP LUNG SURFACTANT

ACTIVE SUBSTANCE INFORMATION

Description:
Surface active agent
Animal lung extract phospholipids and apoproteins
Mechanism of action:
An endogenous pulmonary surfactant that reduces surface tension at the air-liquid interface of the alveoli in the lungs, thus stabilizing them against collapse under trans pulmonary pressures. Pulmonary surfactant in human body is a mixture of lipids and proteins which is secreted into the alveolar space by epithelial type II cells. A deficiency of pulmonary surfactant in premature infants allows surface tension to increase to the point where sections of lung collapse and respiratory distress syndrome (RDS) develops.
Indications:
Respiratory Distress Syndrome (RDS) in premature infants.

ORIGINAL PRODUCT INFORMATION

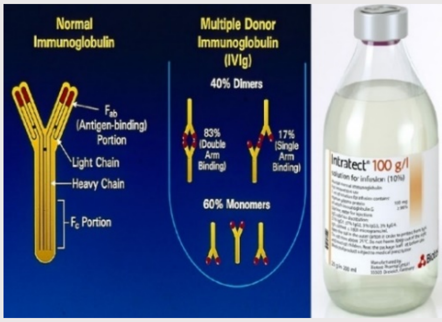
Curosuf (poractant alfa)
Chiesi Farmaceutici, S.p.A.
US patent year: 1979 and 1982
Price and Average Annual Sales:
About ($455 t0 $888)/dose and $270 million/year
Dosage Forms & Strengths:
Instillation Suspension

- 80 mg/ml (1.5 mL and 3 mL vials)

Storage condition:
Refrigeration between 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 12 months.
Startup company: Arnagen Pharmed.
Project stage: Technology is being transferred to Arnagen Pharmed.



HUMAN NORMAL IMMUNOGLOBULIN (IVIG)

PROCESS DEVELOPMENT IN PERSISGEN PAR:

This highly purified product, Intravenous immunoglobulin (IVIG), is prepared from large pools of human plasma and producing process involves several steps that not only enrich the immunoglobulins but also reduces any potential probable viruses.

Purification process includes stages such as centrifugation for cryoprecipitate removing, cryopoor plasma pH adjustment and cryopoor plasma (CPP) clarification, euglobulin precipitation, depth filtration, solvent/detergent treatment for virus inactivation, chromatography steps to IgG capturing and polishing, microfiltration and ultrafiltration /diafiltration and finally viral filtration.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D and industrial scale was the fractionation of 5 and 100 liters of plasma, respectively with 5 to 5.4 gr/L of plasma final yield.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Passive immunizing agent
Plasma derived human immunoglobulin g
Mechanism of action:
Intravenous immunoglobulin (IVIG) products are derived from the pooled human plasma of thousands of donors, ensuring that the IVIG preparation contains a wide diversity of antibody repertoire with the whole array of variable (antigen-binding) regions of antibodies in normal serum. Immune antibodies are critical for replacement therapy in the treatment of primary immunodeficiency disorders (PID), The functional activities of IgG molecules, such as bactericidal effect mediated by complement, viral neutralization, inactivation of toxins and opsonization, are important for the development of an effective immune response against a large range of microorganisms and their toxic products. IVIG products may also trigger powerful immunomodulatory and anti-inflammatory effects in different diseases.
Indications:
Primary immunodeficiency, Secondary Immunodeficiency, Idiopathic thrombocytopenic purpura (ITP), Multifocal Motor Neuropathy (MMN).

ORIGINAL PRODUCT INFORMATION

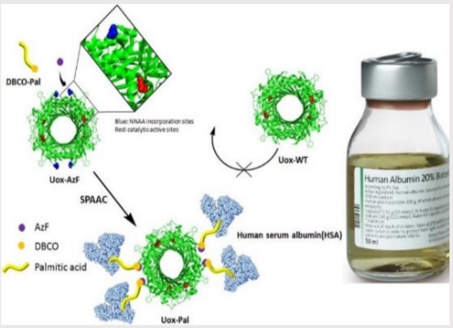
Intratect
Biotest
US patent year: 1980, 1997, 2003 and 2012
Price and Average Annual Sales:
About $41.31/gram and $1.7 billion/year
Dosage Forms & Strengths:
Solution for infusion

- 50 g/l and 100g/l

Storage condition:
Store at 25 °C (room temperature)

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 10 months.
Startup company: Medvac Zist Darou.
Project stage: Technology is being transferred to Medvac Zist Darou and Scaled up to industrial phase by PersisGen Par.



PROCESS DEVELOPMENT IN PERSISGEN PAR:

This product, Human serum albumin (HSA), is a sterile, liquid preparation of albumin derived from large pools of human plasma.

The HSA is produced by a process involves several steps such as centrifugation for cryoprecipitate removing, cryopoor plasma pH adjustment and cryopoor plasma (CPP) clarification, euglobulin precipitation, depth filtration, solvent/detergent treatment for virus inactivation, chromatography steps to human albumin capturing and polishing, microfiltration, ultrafiltration /diafiltration and final container pasteurization.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D and industrial scale was the fractionation of 1 and 100 liters of plasma, respectively with 25 to 30 gr/L of plasma final yield.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

HUMAN SERUM ALBUMIN (HSA)

ACTIVE SUBSTANCE INFORMATION

Description:
Plasma expander
human plasma protein
Mechanism of action:
Human serum albumin (HSA) regulates the transport and availability of numerous chemical compounds and molecules in the blood vascular system. The main function of albumin results from its contribution to plasma colloid oncotic pressure and transport function. Albumin stabilizes circulating blood volume and carries hormones, enzymes, medicines, and toxins. Other physiological functions include antioxidant properties, free radical scavenging, in addition to maintenance capillary membrane integrity. Exogenously administered albumin increases the oncotic pressure of the intravascular system, moving fluids from the interstitial space, thereby decreasing edema and increasing the circulating blood volume.
Indications:
Hypoalbuminemia, Hypovolemia, Prevention of central volume depletion after paracentesis due to cirrhotic ascites (Treatment Adjunct

ORIGINAL PRODUCT INFORMATION

Albiomin
Biotest
US patent year: 1980, 1997, 2003 and 2012
Price and Average Annual Sales:
About ($102.46 to $196.42)/dose and $5381 million/year
Dosage Forms & Strengths:
Solution for infusion

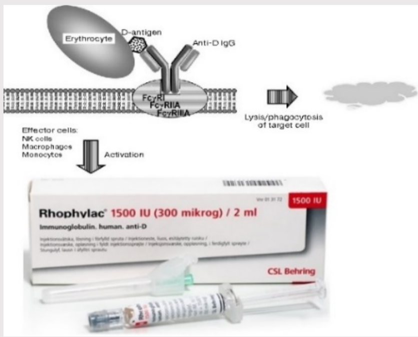
- 50 ml and 100 ml 20% Glass vials

Storage condition:
store below 25°c

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 10 months.
Startup company: Medvac Zist Darou.
Project stage: Technology is being transferred to Medvac Zist Darou and Scaled up to industrial phase by PersisGen Par.

RHO (D) IMMUNE GLOBULIN



PROCESS DEVELOPMENT IN PERSISGEN PAR:

The production process for Rh$_o$ (D) Immune Globulin is sets of several purification and pathogen removal or inactivation techniques including caprylic acid treatment, filtration, ion exchange chromatography, virus removal filtration and diafiltration/ ultrafiltration to obtained high purified immunoglobulin.

All of the above steps are designed to increase the product safety by reducing the risk of pathogen transmission and immunologic reactions.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D scale was the production from 1 liter of plasma. The final yield (potency) was 35 IU/ml of plasma.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Passive Immunizing Agent
Plasma derived human immunoglobulin
suppressing the immune response of Rh-negative individuals to Rh-positive red blood cells
Mechanism of action:
Anti-D works by binding to Rhesus D antigen expressed on red blood cells, which leads to their recognition by Fc receptors on cells of the reticuloendothelial system. The coated red cells compete with the antiplatelet-antibody-coated platelets for the activated Fc receptors, thereby slowing platelet clearance
Indications:
Pregnancy and other obstetrical conditions in Rh-negative women

ORIGINAL PRODUCT INFORMATION

Rhopylac
CSL Behring GmbH.
US patent year: 1976, 1986, 1997 and 2003.
Price and Average Annual Sales:
About $87.97/dose, $82 million/year and $140 million/year in 2024 (for Hyperimmune Globulins)
Dosage Forms & Strengths:
solution for injection pre-filled syringe

- 1500 IU (300 micrograms)

Storage condition:
Refrigeration between 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 13 months.
Startup company: Novin Darou Zist Fanavar Haraz.
Project stage: The technology is transferred to Novin Darou Zist Fanavar Haraz and Scaled up to industrial phase.

PROCESS DEVELOPMENT IN PERSISGEN PAR:

Insulin glargine is a human insulin analogue designed to have a low solubility at neutral pH. It is completely soluble at the acidic pH (pH 4). After injection, the acidic solution is neutralised leading to formation of micro-precipitates from which small amounts of insulin glargine are continuously released and provided a smooth, peak less, predictable concentration/time profile with a prolonged duration of action.
The drug substance produced in Escherichia coli by recombinant DNA technology using fed-batch fermentation. Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale fermentors, respectively, and purification stages including the clarification of harvest, a series of chromatography and polishing and ultra-diafiltration/ filtration steps.
Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well.
The R&D scale was the production in 5 liter fermentor with 5gr/L protein expression.
Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

INSULIN GLARGINE

ACTIVE SUBSTANCE INFORMATION

Description:
A human insulin analogue
Long-acting insulin
Mechanism of action:
The activity of insulin glargine, is regulation of glucose metabolism. Insulin and its analogs lower blood glucose levels by stimulating peripheral glucose uptake, 1 especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis, and enhances protein synthesis. Upon subcuteous injection, the solution is neutralized resulting in the formation of microprecipitates. Small amounts of insulin glargine are released from microprecipitates giving the drug a relatively constant concentration over time profile over 24 hours with no pronounced peak. This release mechanism allows the drug to mimic basal insulin levels within the body.
Indications:
Improve glycemic control in adults and pediatric patients with type 1 diabetes and in adults with type 2 diabetes mellitus.

ORIGINAL PRODUCT INFORMATION

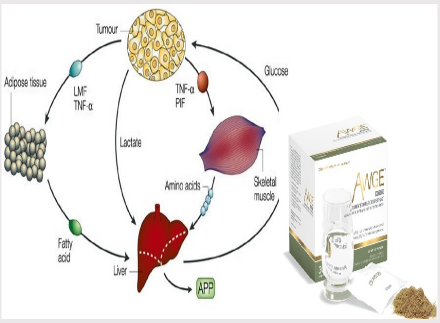
Lantus
Sanofi-Aventis, Inc.
US patent year: 1994, 2003, 2004, 2007 and 2008
Price and Average Annual Sales:
About $30.45/dose, $6044 million/year
Dosage Forms & Strengths:

- Single-use vial: 100 units/ml
- Single-use pre-filled pen: 100 units/ml
- Single-use cartridge: 100 units/ml

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 8 months.
Startup company: Arnagen Pharmed.
Project stage: The technology is ready for transfer.



PROCESS DEVELOPMENT IN PERSISGEN PAR:

The Process Development for this immunostimulatory and metastasis inhibitor, FWGE, includes wheat germ fermentation in an aqueous medium in the presence of Saccharomyces Cerevisiae, the separation of fermented liquid, filtration, evaporating and drying to obtain the resulting final product. Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D scale was the production in 5 liter fermentor. Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

FERMENTED WHEAT GERM EXTRACT (FWGE)

ACTIVE SUBSTANCE INFORMATION

Description:
cancer-fighting and immune supporting supplement
fermented wheat germ extract
Mechanism of action:
FWGE reduces the MHC-I level on human tumor cells and their metastatic activities, makes more ICAM-1 on the cells of the vessels and helping the leucocytes to infiltrate the tumor, blocks ribonucleotide reductase of cancer cells, inhibits PARP and DNA repair in cancer cells, block COX-1 and COX-2 enzymes and relief inflammation
Indications:
Coadministration with anticancer drugs (colorectal, breast, lung, colon, head and neck, oral and pediatric cancers), autoimmune disease.

ORIGINAL PRODUCT INFORMATION

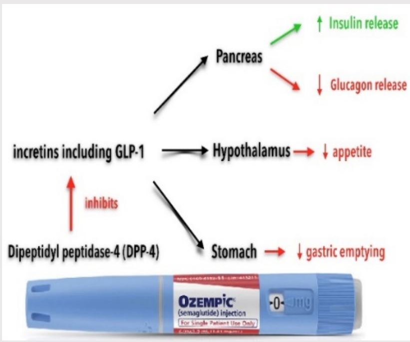
Avemar
Biropharma
US patent year: 2010 and 2012
Price and Average Annual Sales:
About $194.98/300 tabs and $179.99/30 Sachets, $2.04 billion/year
Dosage Forms & Strengths:

- Water soluble granulate sachets (dried fermented wheat germ extract): 17 gram/Sachet
- Film-coated tablets: 1.7 gram/tablet

Storage condition:
Store below 15°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 18 months.
Startup company: Avin Zist Kimia Dadeh.
Project stage: The technology is ready for transfer.



PROCESS DEVELOPMENT IN PERSISGEN PAR:

Semaglutude is a long acting analogue of human glucagon like-1 peptide, acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor.

The drug substance produced in Saccharomyces cerevisiae by recombinant DNA technology using fed-batch fermentation, followed by chemical modifications. Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale fermentors, respectively and purification stages including the clarification of harvest, a series of chromatography and polishing and ultra-diafiltration/ filtration steps.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D and Industrial scale was the production in 5 and 50 liter fermentor, respectively with 1.3 gr/L protein expression.

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SEMAGLUTIDE

ACTIVE SUBSTANCE INFORMATION

Description:
Blood glucose lowering drugs
A human glucagon-like peptide 1 (GLP-1) analogue
A GLP-1 receptor agonist
Mechanism of action:
GLP-1 is a physiological hormone that has multiple actions in glucose and appetite regulation, and in the cardiovascular system. Semaglutide reduces blood glucose in a glucose dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. Semaglutide reduces body weight and body fat mass through lowered energy intake, involving an overall reduced appetite. In addition, Semaglutide reduces the preference for high fat foods. GLP-1 receptors are also expressed in the heart, vasculature, immune system and kidneys. Semaglutide had a beneficial effect on plasma lipids, lowered systolic blood pressure and reduced inflammation and atherosclerosis in clinical studies.
Indications:
To improve glycemic control in adults with type 2 diabetes mellitus

ORIGINAL PRODUCT INFORMATION

Ozempic
Novo Nordisk, Inc.
US patent year: 2002, 2004, 2005 and 2006
Price and Average Annual Sales:
About $814.92/dose, $0.21 billion/year and $4.25 billion/year in 2024
Dosage Forms & Strengths:

- Single-use pre-filled pen 2 mg/1.5 mL (1.34 mg/mL): a pre-filled multidose (0.25 mg, 0.5 mg and 1 mg) disposable pen-injector containing a 1.5 mL cartridge

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 4 months.
Owner: CinnaGen Co.
Project stage: Technology is transferred to CinnaGen Co.

TEDUGLUTIDE

PROCESS DEVELOPMENT IN PERSISGEN PAR:

Tedaglutide is an analogue of human glucagon like-2 peptide, acts as a GLP-2 receptor agonist that increases intestinal and portal blood flow, inhibits gastric acid secretion, and decreases intestinal motility.

The drug substance produced in Escherichia coli by recombinant DNA technology using fed-batch fermentation. Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale fermentors, respectively, and purification stages including the clarification of harvest, a series of chromatography and polishing and ultra-diafiltration/ filtration steps.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D scale was the production in 5 liter fermentor and final yield was 200 mg/L of media culture.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Various alimentary tract and metabolism products
A human glucagon-like peptide 2 (GLP-2) analogue
A GLP-2 receptor agonist
Mechanism of action:
Teduglutide has been shown to preserve mucosal integrity by promoting repair and normal growth of the intestine through an increase of villus height and crypt depth. GLP-2 is known to increase intestinal and portal blood flow, inhibit gastric acid secretion and decrease intestinal motility. Teduglutide binds to the GLP-2 receptors located in intestinal subpopulations of enteroendocrine cells, subepithelial myofibroblasts, and enteric neurons of the submucosal and myenteric plexus. Activation of these receptors results in the local release of multiple mediators, including insulin-like growth factor-1, nitric oxide and keratinocyte growth factor.
Indications:
Short Bowel Syndrome (SBS)

ORIGINAL PRODUCT INFORMATION

Gattex
Hospira, Inc.
US patent year: 1995, 2002 and 2005
Price and Average Annual Sales:
About $41,008/kit, $335.5 million/year and $1 billion/year in 2021
Dosage Forms & Strengths:

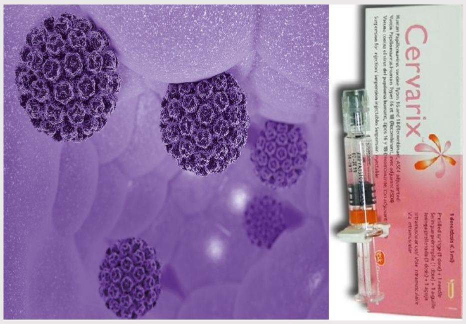
- Single-use vial: 5 mg Lyophilized powder with 0.5 mL of sterile Water (provided in a prefilled syringe)

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 12 months.
Startup company: Protein Fanavar Pajouh.
Project stage: The technology is ready for transfer.

HUMAN PAPILLOMAVIRUS (HPV) VACCINE



PROCESS DEVELOPMENT IN PERSISGEN PAR:

This product, human papillomavirus (HPV) vaccine, is an adjuvant non-infectious recombinant vaccine prepared from the highly purified virus like particles (VLPs) of the major capsid L1 protein of oncogenic HPV types 16 and 18.
L1 protein in the form of non-infectious virus-like particles (VLPs) produced by recombinant DNA technology using an adjuvant system composed of synthetic MPL and aluminum salt.
Production process contains cell culture stages including culturing in plates, shaker flasks, and bench-scale wave bioreactors, respectively, and purification stages including cell lysis and clarification of harvest, a series of chromatography, polishing and several filtration steps.
Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well.
The R&D and industrial scale was the production in 5 and 50 liter bioreactor, respectively and the productivity was 8000 dose per each 25 liter bioreactor.
Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Vaccines, Papillomavirus vaccines
An adjuvanted non-infectious recombinant vaccine
Mechanism of action:
HPV vaccine is a non-infectious recombinant vaccine that contains recombinant L1 protein, the major antigenic protein of the capsid, of oncogenic HPV types 16 and 18. It is thought that the efficacy of the vaccine may be mediated by the development of IgG neutralizing antibodies directed against HPV-L1 capsid proteins generated as a result of vaccination.
Indications:
Premalignant ano-genital lesions (cervical, vulvar, vaginal and anal)
Cervical cancer
Cervical intraepithelial neoplasia (CIN) Grade 2 or worse and adenocarcinoma in situ
Cervical intraepithelial neoplasia (CIN) Grade 1.

ORIGINAL PRODUCT INFORMATION

Cervarix
GlaxoSmithKline (Gsk) Biologicals s.a., Inc.
US paten year: 2000
Price and Average Annual Sales:
About $250/dose, $3151 million/year and ($5 to$7) billion/year in 2025
Dosage Forms & Strengths:

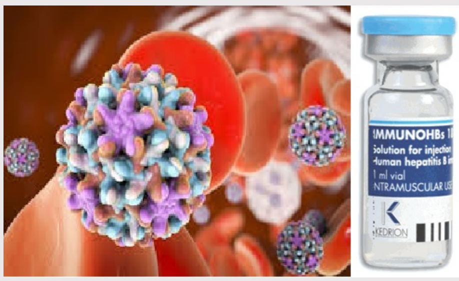
- Single-use pre-filled syringe: A 0.5-mL suspension for injection

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 10 months.
Startup company: Noyan Pajouhan BioPharm.
Project stage: Technology is being Scaled up to industrial phase for the production of drug substance in PersisGen Par CDMO facility and drug product by Noyan Pajouhan BioPharm.

HUMAN HEPATITIS B IMMUNOGLOBULINE



PROCESS DEVELOPMENT IN PERSISGEN PAR:

Human hepatitis B immunoglobulin contains mainly immunoglobulin G (IgG) with a specifically high content of antibodies against hepatitis B virus surface antigen (HBs). The polyclonal IgG is prepared from the plasma of donors which hyperimmunized with hepatitis B vaccine.

The drug substance production includes sets of several purification and pathogen removal or inactivation techniques such as caprylic acid precipitation, filtration, ion exchange chromatography, virus removal filtration and diafiltration/ultrafiltration to obtained purified immunoglobulin.

All of the above steps are designed to increase the product safety by reducing the risk of pathogen transmission and immunologic reactions.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well.

The R&D scale was the production from 1 liter of plasma and final yield was 3.5-4 IU/ml of plasma.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Anti-infectious, Immune sera and immunoglobulin
A solution of human hepatitis B immunoglobulin
Anti-hepatitis B virus surface antigen (HBs).
Mechanism of action:
The pooled monomeric IgG present in HBIg provides a variety of antibodies capable of neutralizing the hepatitis B virus by opsonization, resulting in complement activation and stimulation of cell-mediated immunity. The passive immunity imparted by HBIg is capable of attenuating or preventing HBV infection.
Indications:
hepatitis B
hepatitis B virus infection after liver transplantation

ORIGINAL PRODUCT INFORMATION

ImmunoHBs
Kedrion S.p.A., Inc.
US patent year: 1974, 1975, 1978, 1980, 1983, 1997 and 2003
Price and Average Annual Sales:
About $36.67/dose, $82 million/year and $140 million/year in 2024 (for Hyperimmune Globulins)
Dosage Forms & Strengths:

- Single-use vial: 180 IU/ml
- Single-use vial: 540 IU/ml

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 10 months.
Startup company: Novin Darou Zist Fanavar Haraz.
Project stage: The technology is transferred to Novin Darou Zist Fanavar Haraz and Scaled up to industrial phase.

PROCESS DEVELOPMENT IN PERSISGEN PAR:

Human rabies immunoglobulin (RIG) contains mainly immunoglobulin G (IgG) with a specifically high content of antibodies against rabies virus.

The drug substance contains human protein including mainly IgG. Human RIG (HRIG) derived from immunized humans. The polyclonal RIGs is prepared from the plasma of donors which hyperimmunized with rabies vaccine. The purification process of HRIG contains sets of steps including caprylic acid treatment, filtration, ion exchange chromatography, virus removal filtration and diafiltration/ ultrafiltration to obtained high purified immunoglobulin.

All of the above steps are designed to increase the product safety by reducing the risk of pathogen transmission and immunologic reactions.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D scale was the production from 1 liter of plasma and final yield was 3.7-4 IU/ml of plasma.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization, ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

HUMAN RABIES IMMUNOGLOBULIN

ACTIVE SUBSTANCE INFORMATION

Description:
Immune sera and immunoglobulin: Human rabies immunoglobulin
Medicinal product derived from human plasma
Mechanism of action:
Rabies immune globulin binds and neutralizing the rabies virus, preventing it from invading the central nervous system and provides passive. Rabies immune globulin provides immediate passive antibodies for a short period of time. This protects the patient until the patient can produce active antibodies from the rabies vaccine.
Indications:
Rabies

ORIGINAL PRODUCT INFORMATION

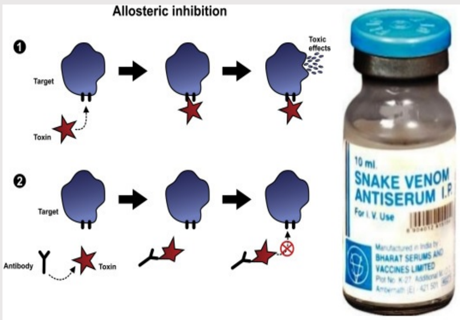
Berirab P
CSL Behring L.L.C., Inc.
US patent year: 1964, 1974, 1984 and 2006
Price and Average Annual Sales:
About $39.68 to $88.33)/dose, $290 million/year and $450 million/year in 2024
Dosage Forms & Strengths:

- A Single vial: 2 mL, 5 mL, 10 mL

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 10 months.
Startup company: Novin Darou Zist Fanavar Haraz.
Project stage: The technology is transferred to Novin Darou Zist Fanavar Haraz and Scaled up to industrial phase.



ANTIVENOM IMMUNOGLOBULIN

PROCESS DEVELOPMENT IN PERSISGEN PAR:

Antivenom immunoglobulin is a mixture of equine-derived antivenin Immune fragments. The product is a sterile preparation of equine immunoglobulin F(ab')2 fragments, produced from the plasma of immunized horses against venom. It can be monovalent and effective against a single species' venom or polyvalent, a range of species or several different species at the same time based on immunization strategy.

The drug substance is obtained by pepsin digestion of horse plasma to remove the Fc portion of immunoglobulin, followed by fractionation and purification steps. The purification process is sets of several techniques including enzymatic digestion, caprylic acid precipitation, several filtration steps such as virus removal filtration and diafiltration/ ultrafiltration.

All of the above steps are designed to increase the product safety by reducing the risk of pathogen transmission and immunologic reactions.

Furthermore, in PersisGen Par providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done. The R&D and industrial scale was the production from 1 and 60 liters of plasma, respectively with 75% productivity.

Development of the CQAs, CPPs, risk assessment and control strategy based on quality target product profile (QTPP) characterization, supported by parallel experimentation, and design of experiment optimization ensure that the route chosen is robust, reliable, and ultimately scalable. In addition, establishment of the process development and design criteria for the product were performed.

ACTIVE SUBSTANCE INFORMATION

Description:
Immune sera and immunoglobulin
Medicinal product derived from animal plasma
Mechanism of action:
Antivenom immunoglobulin contains venom-specific F(ab')2 fragments of immunoglobulin G (IgG) that bind and neutralize venom toxins, facilitating redistribution away from target tissues and elimination from the body.
Indications:
Adult and pediatric patients with venomous species envenomation

ORIGINAL PRODUCT INFORMATION

US patent year: 1984, 1991 and 2000
Price and Average Annual Sales:
The cost in the developing world is US$ (9.00–118.80)/vial. In the United States the cost is about $2,300/dose. The cost in Iran is about $100/vial.
Dosage Forms & Strengths:

- A Single vial: 2 mL, 5 mL, 10 mL

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 6 months.
Startup company: Padra Serum Co.
Project stage: Technology is transferred to Padra Serum Co. by PersisGen Par and scaled up to industrial phase.

DECAPEPTIDE-BASIC FIBROBLAST GROWTH FACTOR (BFGF)

PROCESS DEVELOPMENT IN PERSISGEN PAR:

BFGF is peptide-based lotion preparation, for external use only. It is composed of 10 amino acids (Deca-peptide) and acts as Mitogen to Melanocytes, chemokinetic & chemotactic (thus Melanocytes proliferate at margins and migrate & populate the Vitiligo patch) and a stimulator of pigmentation.

The drug substance is produced from the mixture of peptide and other suitable ingredients like solvents, for topical use and formulated under GMP condition.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well.

ACTIVE SUBSTANCE INFORMATION

Description:
A peptide-based lotion
A combination of 10 amino acids (Deca-peptide)
Mitogen to Melanocytes, Stimulates Pigmentation
Mechanism of action:
BFGF is a cell signaling protein and acts as an important factor in cross-talk between the signaling pathway of proliferation and differentiation of melanocytes. Increasing the numbers of melanocytes causes to restore pigmentation of white patches on the skin.
Indications:
Vitiligo/white patches

ORIGINAL PRODUCT INFORMATION

Melgain
Dr Reddy's & Issar Pharmaceuticals Pvt Ltd, Inc.
US patent year: 1997, 2006.
Price and Average Annual Sales:
About ($10.18 to &18.67)/dose, Global Vitiligo market will be US$ 2.4 Billion by the year 2024.
Dosage Forms & Strengths:

- Single vial with roll-on applicator: 2 mL, 5 mL, 10 mL

Storage condition:
Store below 15°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 1 month.
Startup company: Hivea Zistpoya Alborz.
Project stage: The technology is ready for transfer.

CHLORELLA VULGARIS

PROCESS DEVELOPMENT IN PERSISGEN PAR:

Chlorella vulgaris is a microscopic green algae not much larger than a red blood cell, which is a rich source of natural components including protein, fats, omega-3 polyunsaturated fatty acids, polysaccharides, carbohydrates, fiber, chlorophyll, vitamins, and minerals.
The product is a dried biomass of C. vulgaris, which is cultured in the specific growth medium under controlled conditions of light intensity and temperature in a photo-bioreactor, and then harvested.
The downstream process is sets of several techniques including homogenization and spray drying. Finally, a dried biomass is produced in form of tablets.
Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D and industrial scale was the production in 10 and 80 liter photo-bioreactor, respectively and final yield was 2.4 gr/L of culture media.
In addition, the cell bank with its characterization as well as CTD documents for the final product, is prepared.

ACTIVE SUBSTANCE INFORMATION

Description:
A nutritional supplement and medicine
A green unicellular microalgae
Mechanism of action:
Chlorella is a good source of protein, fats, omega-3 polyunsaturated fatty acids, polysaccharides, carbohydrates, fiber, chlorophyll, vitamins, and minerals. It may act as an antioxidant.
Indications:
Clinical trials and the findings on the health benefits of the molecular mechanisms of Chlorella vulgaris, have suggested that supplementation with this drug can ameliorate amelioration hyperlipidemia and hyperglycemia, and protect against oxidative stress, cancer and chronic obstructive pulmonary disease. It may applied for high blood pressure, high cholesterol, metabolic syndrome, depression, preventing cancer, reducing radiation or chemotherapy treatment side effects, hepatitis C and for a muscle disorder called fibromyalgia.

ORIGINAL PRODUCT INFORMATION

Algomed
Roquette Klötze GmbH & Co. KG
US patent year: 1953.
Price and Average Annual Sales:
About ($34.69 to $189.19)/dose, $49 million/year and $68 million/year in 2024.
Dosage Forms & Strengths:

- Powder : 100% purity
- tablets: 300 milligram/tablet

Storage condition:
Store at 25 °C (room temperature)

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 4 months.
Startup company: Nik Paya Karen Pharmed.
Project stage: Technology is transferred to Nik Paya Karen Pharmed by PersisGen Par and scaled up to industrial phase.

ORAL PROBIOTIC

PROCESS DEVELOPMENT IN PERSISGEN PAR:

Oral Probiotic is a new formulation of probiotics for treatment of periodontal disease that could play a role in Inhibition of pathogen adhesion, colonization and biofilm formation, Induction of expression of cytoprotective proteins on host cell surfaces, Inhibition of collagenases and reduction of inflammation associated molecules, Stimulation and modulation of the host immune system. Probiotics can also modify the surrounding environment by modulating the pH and/or the oxidation–reduction potential, which may compromise the ability of pathogens to become established.

The product is a combination of dried biomass of Lactobacillus plantrum, which is cultured in the specific growth medium under controlled conditions of pH and temperature in a fermentor which harvested after the optimization of bacterial growth curve.

The downstream process is sets of several techniques including homogenization and spray drying. Finally, a dried biomass is formulated using specific excipients in form of tablets.

Furthermore, in PersisGen Par the comparability studies to approve high similarity between reference standard and final product, and providing step-by-step instructions for performing each stage in a facilities operation (SOPs) and documentation, were done, as well. The R&D scale was the production in 2 liter fermentor and the final yield was 3800 tablets per liter of culture media.

ACTIVE SUBSTANCE INFORMATION

Description:
Probiotics for oral and periodontal Health
Mechanism of action:
In periodontal diseases, there is an increase in plaque mass and a shift towards obligatory anaerobic and proteolytic bacteria. The host damage that occurs during periodontal disease arises through the combined activities of subgingival biofilms and the host responses to these diverse bacterial populations. The effect of probiotic tablets on gingivitis and different grades of periodontitis illustrated that probiotic treatment resulted in better microbiota normalization and inhibition of the growth of periodontopathogens. Therefore, probiotics residing in the oral cavity could play a role in the oral ecological balance.
Indications:
periodontal diseases (gingivitis and periodontitis)

ORIGINAL PRODUCT INFORMATION

Blis Probiotics
BLIS Technologies, Inc.
US patent year: 2004, 2006, 2010 and 2012.
Price and Average Annual Sales:
About ($9.99 to $24.95)/dose, $49.4 billion/year and $69.3 billion/year in 2024 (for global probiotics market)
Dosage Forms & Strengths:

- tablets: 2.5 billion CFU

Storage condition:
Refrigeration at 2-8°C

PROJECT INFORMATION

Acceleration phase duration in PersisGen Par: 6 months.
Startup company: Zist Yar Pajouh.
Project stage: The technology is ready for transfer.