Warsaw, 22 August 2022

PRICE INQUIRY No. 8
being conducted as a market assessment study

In connection with the project titled: "*Development of a universal fast-response platform, based on RNA technology, ensuring the national drug and epidemiological safety*", co-funded from the state budget by the Medical Research Agency, Polfa Warszawa S.A., you are kindly requested to submit a bid for specialist consulting services relating to the evaluation, coordination of modifications and approval of completeness of developed and received design specifications, including design quality specifications, i.e. URS, VMP, CS, HAZOP, etc., at the baseline design stage.

I. NAME AND ADDRESS OF THE CUSTOMER

Warszawskie Zakłady Farmaceutyczne Polfa S.A.
ul. Karolkowa 22/24
01-207 Warszawa

II. CONTRACT AWARD PROCEDURE

1. This contract is not subject to the Public Procurement Law of 11 September 2019 (consolidated text: Dz. U. [Journal of Laws] of 2019, item 2019).
2. The procedure is being conducted as an intentional and cost-efficient market assessment study while respecting the following rules:
1) to achieve the best possible outcomes using the allocated resources;
2) to choose the best possible means and methods to meet the pre-defined objectives;
3) to ensure transparency, fair competition and equal treatment of contractors.

III. DESCRIPTION OF THE PRICE INQUIRY

III.1. This Price Inquiry refers to *the provision of specialist consulting services relating to the evaluation, coordination of modifications and approval of completeness of developed and received design specifications, including design quality specifications, i.e. URS, VMP, CS, HAZOP, etc., at the baseline design stage*.

III.2. Description of the project:

Design and release for use of a new research and manufacturing site to be located at ul. Osmańska in Warsaw, which will be comprised of the following areas:

- non-GMP areas: R&D (technological and physical/chemical) laboratories, non-GMP storage space, technical areas plus rest and refreshment facilities;
- GMP areas (physical/chemical laboratory (KJ), microbiological laboratory (KJB), GMP storage space plus a receiving bay and sample collection area, sample retention area, records archive, stability testing site, manufacturing site plus weighing, packing and sterilization rooms).

A description of the site is provided in Appendix 4 hereto. A floor plan of the site, showing the location of the individual areas, is attached in Appendix 5 hereto.

Given the need to design and release for use the above areas, the scope of works will include as follows:

- relocate the existing R&D Laboratory of the sponsor (Fluid Technology Laboratory and Analytical Laboratory plus the provision of space for GMP-KJ Analytical Laboratory);
- relocate and provide additional equipment to the PW Microbiological Laboratory;
- prepare and release for use the GMP Analytical Laboratory;
- design and release for use a GMP manufacturing site, including detailed design specifications for the consecutive operations involved in the manufacture of clinical trial batches and small commercial batches, taking into account product characteristics as well as all process-related activities (Pilot Plant, dosage forms: sterile solutions for injections in vials, sterile solutions for injections in pre-filled syringes (PFS) made from cyclo-olefin polymer (COP), PFS, cartridge – PFS).

The purpose of the project is to obtain a manufacturing authorization and GMP certificate for investigational medicinal products and for the manufacture of small-sized batches of commercial products belonging to the group of antisense oligonucleotides (siRNA), analogs of human oligopeptides, small molecules (for detailed characteristics of reference products and technology, see Appendix 3 hereto).

The required supply utilities available on site:
– electric power,
– potable water ,
– water for injections (WFI),
– purified water (PW),
– clean steam (in-house generator),
– clean/process gases (e.g. nitrogen, compressed air),
– oxygen (non-GMP),
– hot water,
– hot water – HVAC,
– cooling water – HVAC,
– condensate,
– gas.

The project covers the following systems:
– HVAC (AHU, chillers, LAF units, ventilation ducts);
– CIP system (solution preparation line);
– SIP system (solution preparation line);
– toxic wastewater disposal system;
– sewage disposal system;
– RMS;
– BMS;
– PMS;
– AC;
– CCTV;
– UPS;
– PLC;
– electrical wiring (building-wide);
– corporate computerized support systems, i.e. TW, ORACLE, CMMS etc. (to be rolled out in the subsequent stages of the project).

Processing and auxiliary equipment included in the project:
– weighing/sample collection chamber;
– solution preparation system;
– disposable (single-use) solution preparation tanks/set-ups/systems;
– filtration set-up x2;
– filling line (vials/PFS/cartridges);
– automatic parts washer;
– balances;
– autoclave;
– VHP chamber;
– isolator + isolated transport system;
– safety shower (MS);
– mobile LAF unit;
– serialization module.

Toxic substances classified as OEB2 – OEB5 will be handled in laboratories and manufacturing areas. It may be required that APIs/finished products be kept under reduced temperature (for detailed specifications, see Appendix 3).

The manufacturing plant should meet the requirements of:
– EU-GMP, in particular the requirements of Annex 1 'Manufacture of Sterile Medicinal Products' (the draft of the new Annex 1 should also be taken into account);
– US-FDA;
– CA;
– EAU.

The quality, validation and quality documentation should be developed and evaluated based on regulatory acts relating to Good Manufacturing Practices as well as any other standards and regulatory acts applicable to the relevant markets.

III.3. Scope of the Price Inquiry

- Punctual (as per agreed schedule) assessment of submitted design specifications, including in particular the critical aspects in terms of GMP (CDEs, CAs), which might be relevant to the critical quality attributes of the finished product (CQA) or critical process parameters (CPP), e.g. general layout, HVAC layouts, P&ID HVAC, classification layouts, materials/staff/product/waste flow layouts, process flow, process description, equipment layout, utilities layouts, detailed design criteria – HVAC, etc. (for a full list of documents included in the design specifications at the baseline design stage, see Appendix 7 hereto);

- Providing assessments and active participation in the development of qualification and quality documents, i.e. GMP Review, DQ, Containment Strategy, SIA, Validation Master Plan, Risk Analysis, etc. (for a full list of quality / validation documents to be developed / provided with additional information based on reviewed and approved design specifications at the baseline design stage, see Appendix 6 hereto);

- Participation in regular project meetings on site / TC (as necessary and as agreed) organized as part of meetings with designer, general contractor, subcontractors and members of the Design Team or PQC;

- Punctual (as per agreed schedule) assessment of URS prepared upon request (for a full list of URS included in the design specifications at the baseline design stage, see Appendix 8);

- Punctual (as per agreed schedule) assessment of completeness and quality of the design specifications submitted to the Customer at the end of a project stage prior to the official submission for approval;

- Development / assessment of risk analysis, qualification/validation plans, including project qualification in terms of compliance with EU, FDA, CA, EAU requirements;

- Regular communication with and reporting on the progress and results of works to Project Quality Coordinator.

III.4. Skills and experience requirements

a) Experience in similar green-field projects in the pharmaceutical / biotechnological industry or similar high capex projects;
b) English and Polish speaking and writing skills;
c) Knowledge of general EU-GMP, FDA, CA, EAU requirements and those relating to Good Manufacturing Practices as specified in the respective Regulation of Minister of Health, knowledge of the qualification and validation procedures as per Annex 11 and Annex 15 of EU-GMP, CFR requirements and the guidelines applicable in the USA, CA, knowledge of other relevant guidelines, i.e. ISPE (PDA or WHO) GAMP, ISO, ASTM;
d) Knowledge of the EU GMP Annex 1 Revision: Manufacture of Sterile Medicinal Products (Draft) will be an advantage;
e) Hands-on experience in recording and resolving problems related to designing and qualification of areas, GMP-critical systems (e.g. HVAC, water and clean steam systems, clean gases), computer-based systems and equipment;
f) Knowledge in the area of designing areas and preventing cross-contamination as per GMP and EMA's guidelines;
g) Knowledge of specific security requirements for facilities and management standards for high-toxic waste, up to and including the rating of OEB5;
h) General knowledge of control systems, such as RMS/BMS, PMS, which are used for sterile manufacturing processes;
i) General knowledge of computerized systems and data integrity standards;
j) Knowledge in the area of microbiology, supervision of manufacturing processes and sterile areas;
k) Knowledge of manufacturing issues related to industrial operations involved in the manufacture of sterile products using aseptic processes;
l) Knowledge in the field of manufacturing process which is carried out using the RNA technology will be an asset.

A declaration of compliance with the above requirements should be included in the Comments section in Appendix 2 hereto, under your analysis of your compliance with the 'Requirements for contractors' in section V or as a separate appendix to your response to the Price Inquiry.

III.5. Partial bids or variants will not be accepted.

IV. CONTRACT DELIVERY SITE AND DATE

IV.1. The date of delivery for the contract contemplated hereunder: from the date when a contract is signed until 31 December 2022, taking into account an additional period of two weeks for the project qualification (DQ) following formal approval of the design specifications. The qualification process will be considered to have been completed as soon as a report is submitted for approval.

IV.2. The services will be deemed to have been successfully completed when *the design and quality specifications are accepted by the Customer by means of written approval of the documentation, followed by approval of the DQ project qualification report for the BASIC stage*.

IV.3. Place of contract delivery: Warsaw, ul. Barska 31, plus online meetings.

V. REQUIREMENTS FOR CONTRACTORS

V.1. The procedure is open to any Contractors who meet all of the following requirements:

1) Participation in the coordination of two similar green-field projects (design and release for use of GMP manufacturing areas for parenteral dosage forms, including auxiliary laboratories, i.e. Quality Control Laboratory or Biological Laboratory) during the last 4 years, which were successfully completed (implementation and approval following a GMP inspection).

2) Participation in at least 5 projects relating to the validation/qualification of a manufacturing site carrying out aseptic processes.

Assessment procedure:

The submitted bids will be evaluated based on:

a) *The bidder's declaration and list of completed services as per Appendix 2 – dates of completion of services and names of customers.*

b) *CVs of persons who will be involved in the project.*

c) *An additional declaration provided in the Comments section in Appendix 2 or as a separate appendix containing a declaration describing the bidder's compliance with the requirements of section III.4 (you are welcome to include a summary of specific projects you have carried out, including their brief description, to demonstrate that you do have the required specific experience and knowledge).*

V.2. Bids submitted by Contractors who demonstrate that they meet the specified requirements will be taken forward to the bid examination and assessment stage. The compliance with the above requirements will be assessed based on a 'meet – does not meet' basis. Bids submitted by Contractors who fail to meet any of the above requirements will be rejected.

VI. CONTRACT AWARD CRITERIA

VI.1. The following criteria will be used by the Customer for the assessment of bids:
– total net price – 100%

VI.2. The score (P_C) for the Total Net Price will be calculated as follows:

$$P_C = \frac{C_N}{C_B} * 100\ points$$

where:

P_C - score for the Total Net Price
C_N - the lowest total net price based on non-rejected bids
C_B - total net price of the bid under assessment

Bids with the price given in a currency other than PLN will be converted to PLN at the average exchange rate of the National Bank of Poland on the end date of the bid submission period.

VI.3. The maximum score that can be awarded to Bidder is 100 points. Results will be calculated to two decimal places.

VII. PLACE AND DEADLINE FOR SUBMISSION OF BIDS

VII.1. The final deadline for submitting bids is 31 August 2022 by 11:59 p.m.
– bids can be sent in electronic format (a photocopy of signed document) to the following email address: bogdan.oleksiak@polpharma.com.

VII.2. A bid will be considered to have been properly submitted if a complete bid is delivered to the above email address within the time limit stipulated in this section.

VII.3. No bids submitted past the submission deadline will be considered.

VIII. PREPARATION OF BIDS

VIII.1. The Bidder should draw up one bid using the bid form attached as Appendix 1 hereto.

VIII.2. Bids may be modified or withdrawn prior to the end of the time limit for the submission of bids.

VIII.3. Bidders are required to carefully read the information contained in the Price Inquiry.

VIII.4. The costs of preparing and delivering bids will be borne by the respective Contractor.

VIII.5. For any matters related to this Price Inquiry, please contact the Customer through Bogdan Oleksiak, e-mail: bogdan.oleksiak@polpharma.com.

IX. AMENDMENTS TO THE CONTRACT

IX.1. The Customer reserves the right to make material amendments to the contract, as compared to the bid based on which Contractor was awarded the contract, to the following extent and in the following situations:

IX.1.1. To reflect changes in law that affect the delivery of the services covered by the Contract (in particular changes in VAT rates);

IX.1.2. To improve technical parameters of the services covered by the contract in line with new solutions brought about by technological advancements, without any effects on the gross flat rate;

IX.1.3. To extend the deadline for the delivery of the services covered by the Contract due to additional works which need to be carried out to ensure proper delivery of the services covered by the Contract and which the Customer, while exercising due diligence, could not have foreseen beforehand, subject to section IX.1.6 below;

IX.1.4. To extend the deadline for the delivery of the services covered by the Contract due to force majeure event(s), with any consequences of such an extension;

IX.1.5. To change the parameters of the services covered by the Contract without altering the nature of the Contract – technology-related changes, in particular: the need to deliver the services covered by the Contract using other solutions – in terms of technology or materials – than those specified

in the Price Inquiry in the event that the use of the original solutions could lead to non-delivery or improper delivery of the services covered by the Contract, subject to section IX.1.7. below;

IX.1.6. To make changes with respect to additional deliveries or services to be provided by Contractor, which are not covered by the Contract, as long as they are necessary and when all of the following requirements are met: – Contractor cannot be replaced due to economic or technical reasons, in particular relating to the interchangeability or interoperability of equipment, services or systems contracted under the original Contract, – Contractor replacement could cause significant inconvenience or a material increase in costs for the Customer,

– each subsequent change does not exceed 50% of the original Contract net amount;

IX.1.7. To make changes without altering the nature of the Contract, when all of the following requirements are met: – the Contract needs to be changed due to circumstances which could not have been foreseen by the Customer while exercising due diligence,

– the change does not exceed 50% of the original Contract net amount;

IX.1.8. To replace Contractor with a new contractor:

– as a result of merger, division, transformation, bankruptcy, restructuring or purchase of Contractor or its enterprise as long as the new contractor meets the conditions for participation in the procedure, there are no grounds for its exclusion and the change does not result in other material amendments to the Contract,
– as a result of the Customer taking over Contractor's obligations towards its subcontractors;

IX.1.9. To amend the Contract without altering the nature of the Contract, when the total value of the amendments is less than EUR 215,000 and at the same time it is less than 10% of the original Contract net amount.

IX.2. The Customer can also make non-material amendments to the Contract as compared to the bid based on which Contractor was awarded the Contract.

IX.3. Any amendments to the Contract will be made in the form of an annex signed by both parties and will require approval from the Customer.

IX. ADDITIONAL INFORMATION

IX.1. Any costs and expenses incurred in connection with the preparation and submission of bids are to be paid by the respective Bidders.

IX.2. Until the end of the time limit for the submission of bids, the Customer reserves the right to amend or add new information to this Price Inquiry.

IX.3. The submitted bids will remain valid and binding for 30 days from the final date of the time limit for submitting bids.

IX.4. The provision of the contract draft version to be used in the negotiations will be at the sole discretion of the Customer. The draft version will be presented after the Contractor has been selected.

X. LIST OF APPENDICES

The following appendices are attached to this Price Inquiry:

Appendix number	Appendix title
Appendix 1	Bid form
Appendix 2	Declaration of compliance with the eligibility criteria for the participation in the procedure
Appendix 3	Summary of reference product characteristics
Appendix 4	Description of the production area/process
Appendix 5	Floor plan of the site divided into individual areas and information on their surface area
Appendix 6	Full list of qualification/validation and quality documentation included in the scope of the baseline design
Appendix 7	Full list of documents included in the design specifications
Appendix 8	Full list of URS included in the quality/qualification documentation

BID FORM

Bidder:

Name / Company	
Registered office/place of residence/address of the principal place of business	
E-mail address for the Customer to send correspondence related to the Price Inquiry	
NIP [Taxpayer ID Number]	
REGON [Statistical ID Number]	
Phone number	
Contact person for the Customer	

We offer to deliver the contract for ***the provision of specialist consulting services relating to the development, evaluation and implementation of an integrated quality system in a new area for the manufacture of investigational medicinal products*** as per requirements of the Price Inquiry for **the total price of:**

net amount: PLN/EUR* ……

applicable VAT at ……%: PLN/EUR* ……

gross amount: PLN/EUR* ……

(say: ……..……..)

We also declare as follows:

a. We have read the Price Inquiry and appendices thereto and we raise no objections, and we have obtained the information necessary to prepare our bid.

b. Our bid price includes a lump sum remuneration that covers all the obligations of the future Contractor as necessary to deliver the contract referred to hereunder.

c. Our bid will remain valid and binding for 30 days from the final date of the time limit for submitting bids.

d. We are/We are not a related party within the meaning of Commission Regulation (EC) No. 1126/2008.

……	……
(place and date)	(signature(s) of person(s) authorized to submit statements of will on behalf of the Bidder)

Appendix 2 to the Price Inquiry no 8

Customer:
Warszawskie Zakłady Farmaceutyczne
Polfa S.A.

ul. Karolkowa 22/24

01-207 Warszawa

Contractor's Declaration

OF COMPLIANCE WITH THE ELIGIBILITY CRITERIA FOR THE PARTICIPATION IN THE PROCEDURE

By submitting a bid for **the provision of specialist consulting services relating to the development, evaluation and implementation of an integrated quality system in a new area for the manufacture of investigational medicinal products**, we declare as follows:

INFORMATION ON THE CONTRACTOR:

I declare that we meet the conditions for participation in the procedure as specified by the Customer in section V of this Price Inquiry no. 8:

- participation in the coordination of two similar green-field projects during the last 4 years, which were successfully completed (implementation and approval following a GMP inspection);
- participation in at least 5 projects relating to the validation/qualification of a manufacturing site carrying out aseptic processes.

SUMMARY OF PROJECTS

No.	**Scope of green-field project**	**Implementation period** **(from – to)** (day – month – year)	**Customer** (name, address)	**GMP inspection result**
1.				
2.				
3.				
4.				

No.	**Scope of the project relating to the validation/qualification of a manufacturing site carrying out aseptic processes**	**Implementation period (from – to)** (day – month – year)	**Customer** (name, address)
1.			
2.			
3.			
4.			

COMMENTS

…….....…....……, date: ….....…..…...……

.....

(signature of Contractor's representative/agent)

REFERENCE PRODUCT:	**1) Trevicta (EMA) / Invega Trinza (FDA) 3-month treatment** **2) INVEGA HAFYERA™ (6-month paliperidone palmitate)**	**1) Spinraza 12 mg solution for injection**	**2) Leqvio 284 mg solution for injection**	**3) Ozempic (semaglutide) solution for injection in pre-filled pen** **4) WEGOVY (semaglutide) injection, for subcutaneous use – single dose injector**	**OZURDEX 700 micrograms intravitreal implant in applicator**
PACKAGING	**Pre-filled syringe with COP (Cyclo–Olefin–Polymer)**	**Glass vial**	**Pre-filled syringe**	**Cartridge / Pre-filled syringe**	**Intravitreal implant in applicator.** (Disposable injection device, containing a rod-shaped implant. which is not visible. The implant is approximately 0.46 mm in diameter and 6 mm in length)
DETAILED DESCRIPTION OF THE PACKAGING	Pre-filled syringe (cyclic-olefin-copolymer) with a plunger stopper, backstop, and tip cap (bromobutyl rubber)	5 ml in a Type I glass vial with bromobutyl rubber stopper and an aluminium over-seal and plastic cap	1,5 ml solution in PF (glass type I) **(1)** equipped with a plunger (made of fluoretec coated bromobutyl rubber), needle and rigid needle shield **(1)**	1.5 ml or 3 ml glass cartridge (type I glass) closed at the one end with a rubber plunger (chlorobutyl) and at the other end with an aluminium cap with a laminated rubber sheet (bromobutyl/polyisoprene) inserted. The cartridge is assembled into a disposable pre-filled pen made of polypropylene, polyoxymethylene, polycarbonate and acrylonitrile butadiene styrene.	Rod-shaped implant in applicator. The applicator consists of a plunger (stainless steel) within a needle where the implant is held in place by a sleeve (silicone). The plunger is controlled by a lever on the side of the applicator body. The needle is protected by a cap and the lever by a safety tab. The applicator containing the implant is packaged in a sealed foil pouch containing desiccant
STORAGE CONDITIONS (FINISH PRODUCT)	Do not store above 30°C.	Store in a refrigerator (2°C - 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light	This medicinal product does not require any special storage condition. Do not freeze	36 months when stored in a refrigerator (2°C to 8°C) and kept away from the cooling element, protected from light	Medicinal product does not require any special storage conditions.
STORAGE CONDITIONS (API)	store at <-15°C (retest date 3-5 years depends on supplier) (2) Warm to Room Temperature before use. Keep container tightly closed when not in use.	24 months under long term conditions at **-20 ± 5°C** and for up to 6 months under accelerated conditions at 5 ± 3°C	36 months at **-20 ± 5°C**	60 months under long term conditions **at -20 ± 5°C.** Under accelerated conditions at 5 ± 3°C no change over 6 m time was seen	Protect from light. Store below 25C, retest after 3 years.
PURPOSE	Patients must be adequately treated with INVEGA SUSTENNA® (1-month paliperidone palmitate) for at least four months, or INVEGA TRINZA® (3-month paliperidone palmitate) for at least one 3-month injection cycle . Then 6- month paliperidone palmitate.	Used in treatment of spinal muscular atrophy (SMA) – a rare neuromuscular disorder. The recommended dosage is 12 mg (5 ml) per administration. Spinraza treatment should be initiated as early as possible after diagnosis with 4 loading doses on Days 0, 14, 28 and 63. A maintenance dose should be administered once every 4 months thereafter. **(3)**	Is indicated in treatment of adult patient with primary hypercholesterolaemia. The recommended dose is 284 mg inclisiran administered as a single subcutaneous injection: initially, again at 3 months, followed by every 6 months.	Ozempic is indicated for the treatment of adults patient with inadequately controlled diabetes type 2. One injection per week. WEGOVY is indicated for the treatment of adults patient with obesity as an adjunct to low-calorie diet and increased physical activity. One injection per week as long as the treatment last.	Indicated for the treatment of adult patients with: • visual impairment due to diabetic macular oedema (DME) who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy • macular oedema following either Branch Retinal Vein Occlusion (BRVO) or Central Retinal Vein Occlusion (CRVO) • inflammation of the posterior segment of the eye presenting as non-infectious uveitis

REFERENCE PRODUCT:	**1) Trevicta (EMA) / Invega Trinza (FDA) 3-month treatment** **2) INVEGA HAFYERA™ (6-month paliperidone palmitate)**	**1) Spinraza 12 mg solution for injection**	**2) Leqvio 284 mg solution for injection**	**3) Ozempic (semaglutide) solution for injection in <u>pre-filled pen</u>** **4) WEGOVY (semaglutide) injection, for subcutaneous use – <u>single dose injector</u>**	**OZURDEX 700 micrograms intravitreal implant in applicator**
DESCRIPTION OF MEDICINAL PRODUCT	Paliperidone is indicated for maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone. **(4)**	1) Nusinersen is **an antisense oligonucleotide (ASO**) which increases the proportion of exon 7 inclusion in survival motor neuron 2 (SMN2) messenger ribonucleic acid (mRNA) transcripts by binding to an intronic splice silencing site (ISS-N1) found in intron 7 of the SMN2 pre-messenger ribonucleic acid (pre-mRNA). 2) By binding, the ASO displaces splicing factors, which normally suppress splicing. 3) Displacement of these factors leads to retention of exon 7 in the SMN2 mRNA and hence when SMN2 mRNA is produced, it can be translated into the functional full length SMN protein. **(5)**	1) Inclisiran is a cholesterol-lowering, **double-stranded, small interfering ribonucleic acid (siRNA),** conjugated on the sense strand with triantennary N-acetylgalactosamine (GalNAc) to facilitate uptake by hepatocytes. 2) In hepatocytes, inclisiran utilises the RNA interference mechanism and directs catalytic breakdown of mRNA for proprotein convertase subtilisin kexin type 9. This increases LDL-C receptor recycling and expression on the hepatocyte cell surface, which increases LDL-C uptake and lowers LDL-C levels in the circulation. **(6)**	Semaglutide is a long acting analogue of human glucagon like-1 peptide i.e. an Aib8, Arg34-GLP-1(7-37) analogue substituted on the ε-amino group of the lysine residue in position 26 with an (S)-22,40-dicarboxy-10,19,24-trioxo-3,6,12,15-tetraoxa-9,18,23-triazatetracontan-1-oyl side chain. The side chain consists of two 8-amino-3,6-dioxaoctanoic acid (ADO) spacers, one γ-glutamic acid (Glu) spacer, and a fatty diacid (1,18-octadecanedioic acid). **(7)**	One sustained release sterile implantable rod shaped implant containing 700 micrograms of dexamethasone, located in the needle (stainless steel) of a disposable applicator. (8)
DRUG FORM	Suspension for injection	Solution for injection	Solution for injection	Solution for injection	Intravitreal implant
MANUFACTURING PROCES DESCRIPTION	1. Mixing (WFI, PS20, buffer, NaOH, PEG4000) 2. Sterile filtration (0,22 µm) 3. Homogenization (PPP) 4. Bead milling 5. Sterile filtration (40 µm) 6. Homogenization 7. Filling 	1. Receipt and storage of the drug substance at manufacturing site, temperature equilibration of the drug substance 2. Excipient dispensing and WFI water for artificial cerebrospinal fluid preparation 3. Artificial cerebrospinal fluid preparation 4. Active substance concentrate preparation in aCSF in a container, 5. Compounding and mixing to ensure homogeneity 6. Filters are flushed with waters and than with bulk product to reduce bioburden, get rid of leachables 7. Sterilizing filtration, 8. Aseptic vial filling, stoppering and crimping and 9. 100% visual inspection of filled vials	1. Receipt and storage of the drug substance at manufacturing site, temperature equilibration of the drug substance 2. Dissolution of the active substance in WFI 3. pH adjustment with phosphoric acid or sodium hydroxide, 4. Sterilizing filtration, 5. Aseptic pfs filling, 6. Stoppering	1. Dissolution of all excipients and diluted with WFI to obtain the desired weight. 2. Addition of API to the solution 3. pH adjustment by diluted HCl or NaOH 4. Sterile filtration **to stainless steel filling tank** 5. Aseptic filling into sterilized and depyrogenated 1.5 mL cartridge 6. Inspection of cartridges and assemble in the PDS290 pen injector 7. Labelling and packing in cartons	Development program included (1) development an extrusion process to assure content uniformity of the drug in the implant, the dimensional tolerances and physical characteristics that would facilitate the reliable delivery of the implant from the applicator, (2) development a cutting process to assure accurate dosing in the implants, (3) development a loading process and vision system to detect the loaded implant in the applicator system and (4) development a sterilization process to assure that the implant with the applicator was not adversely affected by gamma sterilization. Based on these development studies and manufacturing experience gained during development all critical steps of the manufacturing process have been identified and adequately studied, and appropriate in-process control parameters have been established. Manufacturing process developed for Phase 3 is essentially the same as the

REFERENCE PRODUCT:	**1) Trevicta (EMA) / Invega Trinza (FDA) 3-month treatment** **2) INVEGA HAFYERA™ (6-month paliperidone palmitate)**	**1) Spinraza 12 mg solution for injection**	**2) Leqvio 284 mg solution for injection**	**3) Ozempic (semaglutide) solution for injection in pre-filled pen** **4) WEGOVY (semaglutide) injection, for subcutaneous use – single dose injector**	**OZURDEX 700 micrograms intravitreal implant in applicator**
					one proposed for commercial product. The Phase 3 equipment is also the same as proposed for commercial product except for improvements that have subsequently been introduced to the commercial process. The product is terminally sterilised by gamma irradiation. The specified dose is 25 - 40kGy which is in compliance with the Ph Eur standard requirements. The majority of steps in the Manufacturing process of the medicinal product are performed in a **Grade C environment** resulting in sealed applicator pouches which are than terminally **sterilised by gamma irradiation** and packed in its outer carton.
ASEPTIC PROCESS VS TERMINAL STERILIZATION	Sterilizing filtration (Aseptic proces)	Sterilizing filtration (Aseptic proces)	Sterilizing filtration (Aseptic proces)	Sterilizing filtration (Aseptic proces)	The product is terminally sterilised by gamma irradiation. The specified dose is 25 - 40kGy which is in compliance with the Ph Eur standard requirements
COMMON CRITICAL ELEMENTS IN THE PROCESS	N/A (Disposable sets dedicated to the product)	N/A (Disposable sets dedicated to the product)	N/A (Disposable sets dedicated to the product)	N/A (Disposable sets dedicated to the product)	N/A (Separate manufacturing line and area)
SINGIEL USED ITEMS	NO (Dedicated suspension preparation proces line (homogenizer, mill, homogenizing mixer, peristaltic pump and dedicate equipment for product)	YES	YES	NO (tbd)	N/A (Separate manufacturing line and area)

General description of the production area/process

1. General description

The manufacturing program for the new area will include the manufacture of sterile dosage forms such as solutions and suspensions. Once manufactured, the dosage forms will be dispensed into the following types of containers:

– glass vials

– prefilled syringes

– cartridges.

Additional product data:

- Density: max. 1.2 g/cm^3.
- pH of solutions and suspensions will be in the range of 2-12.
- Viscosity: max. 2000 cP.
- The product may be photosensitive.
- WFI containing ethanol or acetic acid (as a product component) will be used.
- Batch size: max. 20 L

Work plan

It is assumed that the work plan will be as follows:

- 1 shift/day
- 5 working days/week
- 45 working weeks/year.

2. Warehousing and sample collection area

All starting materials (raw materials, immediate and printed packaging materials) will be delivered to the Warehouse through the Receiving Bay and Shipping Bay (room number 0.101), where they will be recorded. Starting materials will be subject to quality control procedures (collection of samples, quarantine). The warehouse is divided into GMP and non-GMP areas. The GMP storage bay will include 110 pallet spaces at three storage levels. In this section of the warehouse, the following areas can be distinguished:

- Raw materials warehouse
- Finished products warehouse
- Packaging materials warehouse
- Printed materials warehouse
- Rejected materials warehouse
- Cold stores.

In the Warehouse, the sample collection room (0.113) will feature the following equipment for the collection of samples of substances classified as OEB<3 materials:

- class C sampling chamber,
- balances.

Samples of highly toxic active substances will be collected in room 0.622 in an isolator. The term ‘critical active substances’ refers to substances classified as OEB ≥ 3 materials.

3. Pilot-scale manufacturing area

The Pilot Plant features space for the installation of the following main processing equipment:

- isolator for the weighing of highly toxic substances, including equipment for isolated transport,
- 2 solution preparation systems (including one disposable (single-use) system),
- devices for filling and closing of products manufactures on the pilot scale within closed Restricted Access Barrier Systems (cRABS),
- freeze-dryer and vial washer (option for future use),
- autoclave and VHP chamber,
- automatic washer,
- protective and laminar air flow systems,
- decontamination shower.

4. Weighing area

The design provides for one common room for the weighing of non-toxic substances – room number (0.629). A room for weighing of excipients and non-critical APIs. Starting materials will be supplied from the GMP Warehouse (0.105) via corridor (0.351), pass box D (0.625) and pass box C (0.626). The corridor (0.351) will belong to the GMP area which is classified as a CNC area. All materials (products/raw materials) intended for use in a GMP area will be transported in a secure manner and inspected outside the area (non-GMP) in accordance with the procedures.

The weighing room for excipients and non-toxic APIs (0.629) will be used for weighing of raw materials classified as OEB<3 materials. Therefore, the following equipment is expected to be provided with a protective air flow solution:

- laboratory balance with a weighing range of up to 100 g,
- balance with a weighing range of up to 1,000 g,
- tabletop balance with a weighing range of up to 10,000 g.

Given the quantity of materials to be weighed, weighing operations will be carried out manually.

Raw materials to be weighed out for a specific production batch will be closed in special containers which can be transported through a pass box out, and then via a production corridor into the solution preparation room (0.622).

Highly toxic APIs contained in the manufacturer's pre-cleaned original packaging will be transported into the solution preparation room featuring an isolator (0.622), located in the Pilot Plan, through pass boxes (0.603, 0.604). The isolator will be provided with the following balances:

- laboratory balance with a weighing range of up to 100 g,
- tabletop balance with a weighing range of up to 3 kg.

Given the need to weigh out small quantities of active materials, weighing operation in an isolator will be carried out manually. The materials weighed out into containers provided with a divided valve will be transferred for further processing. Any remaining unused materials will be secured in the isolator with additional packaging, removed from the isolator, labelled in accordance with the procedures and transported back to the warehouse. Once the weighing process is completed, the isolator will be washed using a WIP system.

5. Solution preparation operations

There will be two systems in the solution preparation room (0.622):

- disposable (single-use) solution preparation system,
- system for preparation of solutions/suspensions in steel tanks.

Given the specific nature of work in such areas, the solution preparation system will make it possible to use any configuration of connections between tanks. Solutions will be prepared under laminar air flow (LAF) conditions. Tanks will be provided with heating and cooling jackets and tensometric balances. Two tanks will be provided with magnetic stirrers and one with an anchor agitator. Depending on the configuration required due to the technology, tanks will be connected using flexible cables or stainless steel pipes. Once pre-filled with water for injections, the solution preparation tank or homogenizer will be manually loaded through a hatch, funnel with substances classified as OEB<3 materials. It is expected that ethanol, acetic acid (product component) will be used on the line. During the preparation of a solution, alcohol will be added manually to the tank and it may constitute no more than 10% of the total volume of the product.

Dosing operations will be carried out through a hatch. Only after low-toxicity substances are loaded, highly toxic APIs will be added using a system for isolated transport. Toxic substances (OEB≥3) will be loaded using a container provided with the passive side of a divided valve connected to a stub pipe of the solution preparation tank or homogenizer provided with the active side of the valve. During control operations critical processing parameters will be recorded automatically (i.e. solution temperature in the tank, pressure in the tank, transfer pressure, stirring speed, readings of sensors installed on the tanks). Once prepared, the solution will be pumped using compressed gas (nitrogen or compressed air) towards the filling line which will be located in a class B room (0.618). The filtration set-up will consist of:

- pre-filter, 0.45 µm
- sterilizing filter, 0.2 µm.

The suspension preparation process will involve the transfer of a solution through the wall into the filling operations room, and then the solution will be homogenized in the existing homogenizer, following which the solution will be fed under recirculation conditions (within class B filling operations room).

All materials will be transferred into filling rooms (0.617 and 0.618) using two methods:

- VHP chamber – pre-sterilized materials secured with double paper sleeves, i.e.: sterile raw materials;
- pass-through autoclave – materials secured with double paper sleeves:

o stoppers and caps,

o removable components of filling machines,

o small buffer tank, filters, flexible connections, etc.

Materials will be removed outside through:

- Pass box: (finished product).
- Pass box:

Packaging materials/machine components will be transported on trolleys within the area using a multi-bag solution for protection during transport. Materials will be unloaded from the autoclave or VHP chamber under LAF conditions.

6. Filling operations

Products will be filled into the following immediate packages:

– vials

– prefilled syringes

– cartridges.

For products to be packaged in vials, freeze-drying of these solutions will be possible in the future. Finished solutions will be transported into the filling operations area through a port in the wall and a set of filters directly into the filling line. It should be possible to carry out filling and closing operations in a protective nitrogen atmosphere. All operations involving an open product, such as filling, stoppering and transporting of vials to/from the freeze-dryer will be carried out under laminar air flow conditions – class A. Between the freeze-dryer loading area and the filling, closing and capping area, there should be ports/passages to allow two-way transfer of materials, i.e. transferring partially stoppered vials from the filling and closing area into the freeze-dryer, and transferring fully stoppered vials from the freeze-dryer back to the capping area. Once filled and closed, containers will be transported directly to room 0.623 which is the outside washing room and unloading area – vials and cartridges. Pre-filled syringes will be collected directly under class B conditions in the filling operations room. A final sterilization step is not required.

7. IPC

The following parameters will be tested at the laboratory IPC 0.620:

- pH
- viscosity
- osmolality
- packaging weight

- packaging integrity.

8. Equipment washing operations

Dirty accessories to be washed will be transported to the dirty equipment warehouse (0.611). Next, the accessories will be transferred to the washing room and clean equipment warehouse (0.610), where small accessories will be washed in a pass-through washer and large accessories – in a large capacity washing station. Clean accessories will be transferred (large accessories will be transported on trolleys) and stored in the clean equipment warehouse room (0.609). This room will also feature the unloading side of the pass-through washer. Once washed and dried, the accessories that need to be sterilized will be packed into double paper sleeves.

Tanks for solution preparation and the homogenizer will be provided with in-house sets for washing and sterilization on site – CIP/SIP located in the technical area on the first floor. The outside surface of tanks will be washed manually on site. The filling line in the Pilot Plant will enable providing the CIP/SIP option in the future. Until the CIP/SIP system is installed, removable elements of the line will be washed in the washing room and sterilized in an autoclave or VHP chamber.

9. Final packing operations

Packing operations in the Pilot Plant will be carried out manually, divided into the following stages:

- inspection (visual inspection),
- labelling,
- packing into individual cardboard boxes, together with a leaflet,
- serialization,
- packing into bulk boxes.

100% vials found to have the following defects should be rejected:

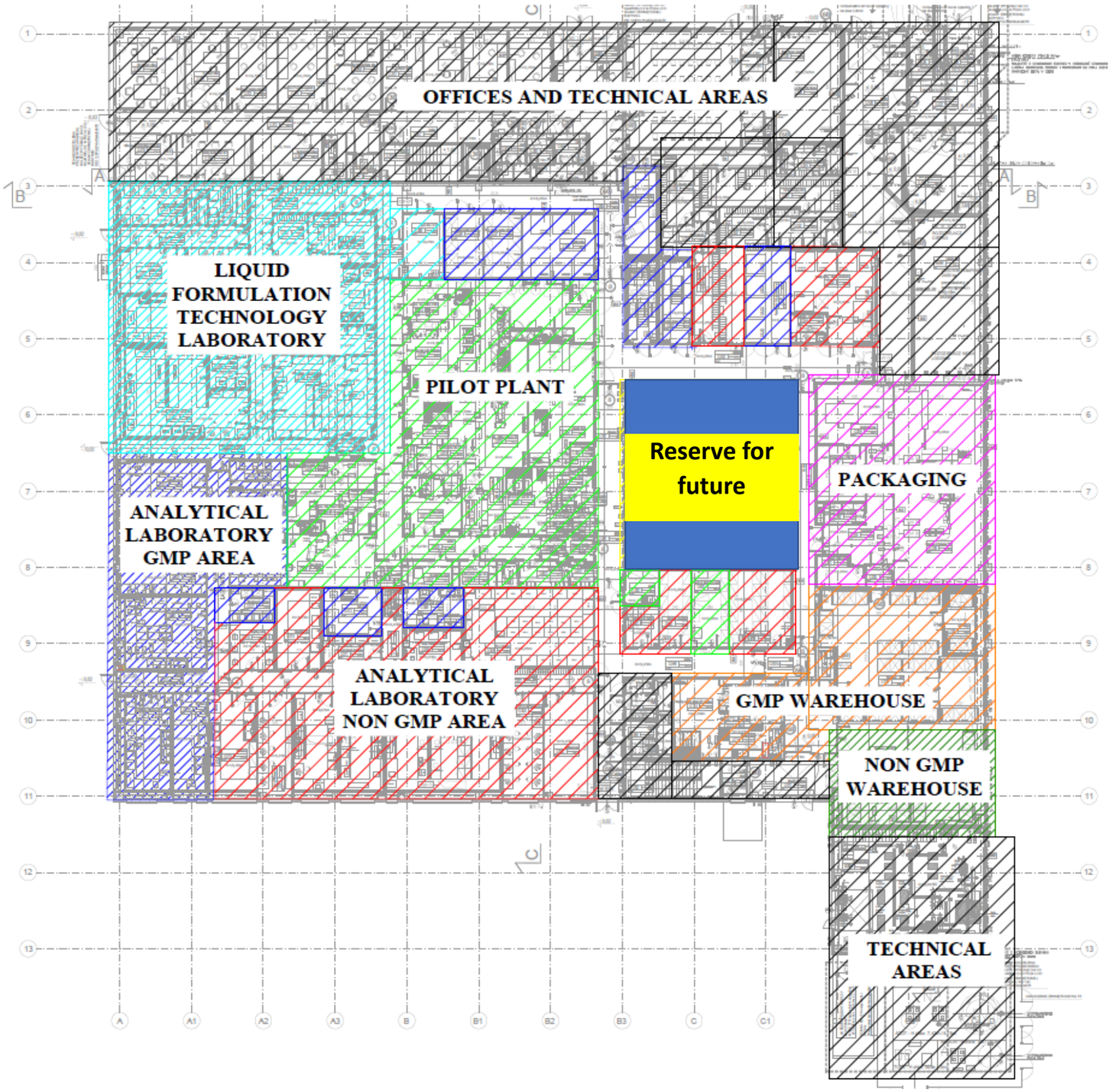
1) Caps/stoppers for closing vials (packaging):

- position and color of a flip-off cap,
- color of a cap,
- missing stopper,
- dented or scratched cap,
- defective cap sealing,
- scratches, cracks, dirt on walls and the bottom.

2) Solutions (product):

- moving particles (glass, metal, fibers),
- floating particles,
- heavy particles at the bottom of a vial,
- liquid level.

Packing operations for products that require dedicated packaging and cannot be packed manually will be outsourced to outside providers. A serialization module will be used for the serialization process. To minimize the risk of confusion between batches/products, packaging operations will be carried out only for one batch at a time, in conformity with POLFA’s internal procedures. Materials required for packaging operations – labels, cardboard boxes, leaflets, bulk boxes will be delivered from the Warehouse directly to the secondary packaging operations rooms, where they will be placed on appropriate devices or moved onto buffer surfaces provided in these rooms. Bulk boxed containing finished products will be stacked onto pallets. Pallets will be transported via pass box number 0.205 to the GMP Warehouse 0.105.



GROUND FLOOR:	
FUNCTIONAL AREA:	**SURFACE [m2]:**
Pilot Plant	522
Secondary Packaging	214
GMP Warehouse	238
Non-GMP Warehouse	92
Liquid Formulation Technology Laboratory	427
Analytical Laboratory GMP Area	485
Analytical Laboratory Non-GMP Area	635
Offices, Technical and Common Areas	1 552
Total Ground Floor R&D & Pilot Plant:	4 165
Reserve for future	194

***Paliperidone is out of main scope of the project for execution phase**

VALIDATION		
No.	**AREA/DRAWING TITLE**	**DESIGN BASIC 2**
		YES/NO
1	Update of the Master Validation Plan – single preparation of the document at the Basic2 stage.	YES
2	Update of the System Impact Assessment (SIA) – single preparation of the document at the Basic2 stage.	YES
3	Update of the Risk Analysis – double preparation of the document at the Basic2 stage.	YES
4	Update of the DQ Plan – single preparation of the document at the Basic2 stage.	YES
5	Update of the DQ Plan – GMP Review – single preparation of the document at the Basic2 stage.	YES
	Update of appendices to the DQ Plan – GMP Review – double preparation of the document at the Basic2 stage.	YES
7	Update of the DQ Plan – URS Review – single preparation of the document at the Basic2 stage.	YES
8	Update of appendices to the DQ Plan – URS Review – double preparation of the document at the Basic2 stage.	YES
9	Update of the DQ Plan – GMP Eurasia Review – single preparation of the document at the Basic2 stage.	YES
10	Update of appendices to the DQ Plan – GMP Eurasia Review – single preparation of the document at the Basic2 stage.	YES
11	Update of the DQ Plan – GMP FDA Review – single preparation of the document at the Basic2 stage.	YES
12	Update of appendices to the DQ Plan – GMP FDA Review – single preparation of the document at the Basic2 stage.	YES
13	Update of the DQ Plan – GMP CA Review – single preparation of the document at the Basic2 stage.	YES
14	Update of appendices to the DQ Plan – GMP CA Review – single preparation of the document at the Basic2 stage.	YES
15	Development of the final DQ report	YES
16	Containment Strategy	YES

No.	AREA/DRAWING TITLE	DESIGN BASIC 2
		YES/NO
1	2	3
ARCHITECTURE		
	FLOOR PLANS	
1	Ground floor plan	YES
2	1st floor plan	YES
3	2nd floor plan	YES
4	Roof plan	YES
5	Machine foundations plan	YES
	SECTIONAL VIEWS	
6	SECTION A-A, B-B	YES
7	SECTION C-C, D-D	YES
	ELEVATIONS	
8	ELEVATIONS	YES
	FLOORING	
9	FLOORING PLAN – GROUND FLOOR	YES
10	FLOORING PLAN – FLOOR 1	YES
11	FLOORING PLAN – FLOOR 2	YES
	DETAILED VIEW OF FLOORING	
12	DETAILED VIEW OF TONGUE EDGE	NO
13	DETAILED VIEW OF FLOOR AND WALL CONNECTIONS	NO
	CEILINGS	
14	CEILING PLAN – GROUND FLOOR	YES
15	CEILING PLAN – FLOOR 1	YES
16	CEILING PLAN – FLOOR 2	YES
	CEILINGS	
17	DETAILED VIEW OF CEILING AND WALL CONNECTIONS	NO
	WALL FINISHING	
18	GROUND FLOOR PLAN – WALL FINISHING	YES
19	1ST FLOOR PLAN – WALL FINISHING	YES
20	2ND FLOOR PLAN – WALL FINISHING	YES
	CLEAN ROOMS	
21	GROUND FLOOR PLAN – CLEAN ROOMS	YES
	CLEAN ROOMS	
22	DETAILED VIEW OF CLEAN WALL	NO
	EQUIPMENT TRANSPORT	
23	EQUIPMENT TRANSPORT	YES
	STAIRCASES	
24	STAIRCASE I	NO
25	STAIRCASE II	NO
26	STAIRCASE III	NO
27	STEEL STAIRS AND TECHNICAL RAMPS	NO
	SUMMARIES	
28	LIST OF INTERIOR DOOR JOINERY WORKS	YES
29	LIST OF GLAZED STRUCTURES	YES
30	LISTING OF STEEL ACCESSORIES AND ELEMENTS – HANDRAILS AND RAILINGS	YES
31	LISTING OF STEEL ACCESSORIES AND ELEMENTS – STEEL LADDERS	YES
32	LIST OF BATHROOM WHITEWARE	NO
33	LIST OF INTERIOR DOOR MATS	NO
34	LIST OF WINDOW SILLS	NO
35	LIST OF INTERIOR METAL WORKS	NO
36	LIST OF SHAFT INSPECTION HOLES	NO
	INTERIOR SPACES	
37	TYPICAL PASS BOX	NO
38	TOILET FACILITIES NO. 1	NO
39	TOILET FACILITIES NO. 2	NO

40	DUST REMOVAL CHAMBER	NO
41	COLD STORE	NO
42	FRONT DESK	NO
43	CANTEEN	NO
44	KITCHEN	NO
	FIRE SAFETY LAYOUT PLANS	
45	LAYOUT OF FIRE PARTITIONS – GROUND FLOOR	YES
46	LAYOUT OF FIRE PARTITIONS – FLOOR 1	YES
47	LAYOUT OF FIRE PARTITIONS – FLOOR 2	YES
48	DESCRIPTION OF WOP	YES
49	SECTIONAL VIEW – FIRE COMPARTMENTS	YES
50	FIRE SCENARIO	NO
	ROOM LIST	
51	ROOM LIST	YES
	DESCRIPTIONS AND SPECIFICATIONS	
52	DESCRIPTION	YES
53	SPECIFICATIONS – PAINTING OF WALLS	YES
54	SPECIFICATIONS – SUSPENDED CEILINGS	YES
55	SPECIFICATIONS – PVC FLOORING	YES
56	SPECIFICATIONS – FITTED CARPETS	YES
57	SPECIFICATIONS – INTERIOR PLASTER WORKS	YES
58	SPECIFICATIONS – WALLS AND PLASTERBOARDS	YES
59	SPECIFICATIONS – CLEAN ROOMS	YES
60	SPECIFICATIONS – PHARMACEUTICAL DOORS AND WALLS	YES
61	SPECIFICATIONS – OFFICE FURNITURE	YES
62	SPECIFICATIONS – INOX AND LABORATORY FURNITURE	YES
63	MTO	YES

STRUCTURAL DESIGN		
1	MACHINE FOUNDATIONS	YES
2	DESCRIPTION	YES
	STEEL STRUCTURAL COMPONENTS	
3	INTERNAL RAILINGS	YES
4	STRUCTURE OF INTERNAL STAIRS – TECHNICAL STAIRCASE	YES
5	STRUCTURE OF STAIRS, INTERNAL LANDINGS AND RAMPS	YES
6	FRAMES FOR ROOF-MOUNTED EQUIPMENT	NO
7	DETAILED VIEW OF SUSPENSIONS FOR SYSTEMS	NO
8	SUBSTRUCTURE FOR THE ENCLOSURE OF DUST REMOVAL CHAMBER AND COLD STORE	NO
9	SUPPORT SUBSTRUCTURE FOR CHIMNEYS	NO
10	DETAILED VIEW OF INSTALLATION SITES (at ceiling +1)	NO
11	DETAILED VIEW OF GIRDER REPLACEMENTS / CHANGES PRIOR TO THE INSTALLATION OF SYSTEMS	NO

MECHANICAL		
1	List of equipment using process utilities	YES
2	Material specifications for CSV pipes	YES
3	Heat distribution room (heat from the heating system) – summary	YES
4	Chilled water system plant room (chilled water system) – summary	YES
5	Steam systems – summary	YES
6	Gas systems – summary	YES
7	Chilled water systems – summary	YES
8	Process heat systems – summary	YES
9	List of heat gains from the designed equipment	YES
10	List of CHW (chilled water) delivery points	YES
11	List of NG (natural gas) delivery points	YES
12	List of HS (clean steam for humidification) delivery points	YES
13	List of ST (process steam) delivery points	YES
14	Material specifications for CSV pipes	YES
15	Technical description of heating and cooling systems	YES
16	Technical description of steam systems	YES
17	Technical description of gas systems	YES
18	Ground floor plan. Heating, cooling and process heat systems	YES
19	1st floor plan. Heating, cooling and process heat systems	YES
20	2nd floor plan. Heating, cooling and process heat systems	YES
21	Roof plan. Cooling system	YES
22	Process heat diagram for air handling units	YES
23	Chilled water diagram for air handling units	YES
24	Diagram of cooling system for the office space	YES
25	Diagram of chilled water system connection to the technology	YES
26	ST process steam system diagram	YES
27	PS clean steam system diagram	YES
28	Ground floor plan. Process steam, clean steam and gas systems	YES
29	1st floor plan. Process steam, clean steam and gas systems	YES
30	Heat distribution functional diagram	YES
31	CDW diagram	YES
32	CHW diagram	YES
33	Steam boiler technical diagram	YES
34	Gas system diagram	YES
35	Chilled water diagram. Fan coil units and duct coolers	YES
36	Process heat diagram. Radiator heating	YES
37	Process heat diagram. Duct heaters	YES
38	Model, scope: process steam, clean steam for humidifiers and gas systems.	YES
39	Model, scope: process steam, clean steam for humidifiers and gas systems.	YES
40	Model, scope: heating systems	YES
41	Model, scope: heating systems	YES
42	Model, range: chilled water systems	YES
43	Model, range: chilled water systems	YES
44	Cooling system plant room number 0.358. Floor plan and sectional view	YES

45	Heating substation number 0.341. Floor plan and sectional view	YES
46	Steam boiler room 1.318b. Floor plan and sectional view	YES
47	Heating, cooling and process heat systems. Sectional views in the air handling unit plant room number 1.318	YES
48	Process steam system. Detailed parts drawings	YES
49	Steam boiler room – summary of materials	YES
50	Diagram of connections between steam/condensate system and receiver units, in particular to air handling units	YES
51	Detailed view of equipment connections (location of shafts/panels in clean rooms)	YES
52	Detailed view of cooling pipes on the roof (including the points where pipes run through the roof)	YES
53	Detailed view of steam pipes on the roof (including the points where pipes run through the roof)	YES

HVAC		
	FLOOR PLANS	
1	Floor plans for the ground floor, 1st floor, 2nd floor and HVAC system areas	YES
2	Ground floor plan, classification of individual areas – clean rooms	YES
3	Ground floor plan, pressure cascade	YES
4	Ground floor plan, ventilation and air-conditioning systems, part 1/2	YES
5	Ground floor plan, ventilation and air-conditioning systems, part 2/2	YES
6	1st floor plan, ventilation and air-conditioning systems, part 1/2	YES
7	1st floor plan, ventilation and air-conditioning systems, part 2/2	YES
8	2nd floor plan, ventilation and air-conditioning systems	YES
9	Roof plan, ventilation and air-conditioning systems, part 1/2	YES
10	Roof plan, ventilation and air-conditioning systems, part 2/2	YES
	SECTIONAL VIEWS	
11	SECTION A-A, B-B	YES
12	SECTION C-C, D-D	YES
	DIAGRAMS	
13	P&ID DIAGRAMS FOR VENTILATION SYSTEM	YES
14	GLYCOL RECOVERY SYSTEM DIAGRAM	YES
15	AIR-CONDITIONING SYSTEM DIAGRAM	YES
	DESCRIPTION, SUMMARIES, SELECTION CARDS	
16	TECHNICAL DESCRIPTION	YES
17	DESIGN ASSUMPTIONS/LIST OF ROOMS AND AREAS (DDC)	YES
18	MATERIAL SPECIFICATIONS (NARRATIVE DESCRIPTION)	YES
19	LIST OF MATERIALS (MTO)	YES
20	SELECTION CARDS FOR AIR HANDLING UNITS	YES
21	SELECTION CARDS FOR DUCT EXCHANGERS	YES
22	DUST COLLECTOR SELECTION CARD	YES
23	SELECTION CARDS FOR BIBO FILTERS	YES
24	CATALOGUE CARDS OF FREON-BASED AIR-CONDITIONING UNITS	YES
25	SELECTION CARDS FOR LAMINAR AIR FLOW SOLUTION	YES
26	SELECTION CARDS FOR GLYCOL RECOVERY PUMPS	YES
27	SELECTION CARDS FOR FANS	YES

WATER & SEWAGE		
	FLOOR PLANS	
1	Municipal water system. Level 0 floor plan	YES
2	Municipal water system. Level +1, +2 floor plan	YES
3	Firefighting water supply system – ground floor	YES
4	Firefighting water supply system – floor +1, +2	YES
5	Underfloor process wastewater disposal system and sanitary sewage system. Level 0 floor plan	YES
6	Process wastewater disposal system and sanitary sewage system. Level 0 floor plan	YES
7	Process wastewater disposal system and sanitary sewage system. Level +1 floor plan	YES
8	Process wastewater disposal system and sanitary sewage system. Level +2 floor plan	YES
9	Process wastewater disposal system and sanitary sewage system. Roof plan	YES
	DIAGRAMS	
10	Municipal water system. Diagram	YES
11	Firefighting water supply system – diagram	YES
12	Sanitary sewage system. Diagram	YES
13	SC1 process wastewater disposal systems. Diagram	YES
14	SC2 process wastewater disposal systems. Diagram	YES
15	P&ID diagram of SC1 process wastewater disposal system	YES
16	P&ID diagram of SC2 process wastewater disposal system	YES
	PROFILES	
17	Underfloor sanitary sewage system. KS1 system. Profile	YES
18	Underfloor sanitary sewage system. KS2 system. Profile	YES
19	Underfloor SC1 process wastewater disposal system. Profile	YES
20	Underfloor SC2 process wastewater disposal system. Profile	YES
21	Underfloor SC2 process wastewater disposal system – hot wastewater. Profile	YES
	SUMMARIES	
22	Municipal water system plus sanitary sewage system and process wastewater disposal system – MTO	YES
23	Firefighting water system – MTO	YES
	SPECIFICATIONS	
24	Specifications of the elements of process wastewater disposal systems	YES
25	Specifications of the elements of sanitary sewage system, sanitary and firefighting water systems	YES
	DESCRIPTION	
26	Municipal and firefighting water systems plus sanitary sewage system and process wastewater disposal system – description	YES

CLEAN MEDIA & GASES		
1	SW and PW generation system. P&ID diagram	YES
2	SW storage and distribution system. P&ID diagram	YES
3	PW storage and distribution system. P&ID diagram	YES
4	WFI generation, storage and distribution system. P&ID diagram	YES
5	Clean steam generation and distribution system. P&ID diagram	YES
6	Compressed air generation system. P&ID diagram	YES
7	Compressed air distribution system. P&ID diagram	YES
8	Nitrogen storage and distribution system. P&ID diagram	YES
9	Oxygen storage and distribution system. P&ID diagram	YES
10	Location of compressed air generation units in room 1.321. Layout plan	YES
11	Location of clean utilities equipment in rooms 1.326 and 1.327. Layout plan	YES
12	Technical specifications. Soft water (SW) and purified water (PW) generation, storage and distribution systems	YES
13	Technical specifications. Water for injections (WFI) generation, storage and distribution system	YES
14	Technical specifications. Clean steam generation and distribution system.	YES
15	Technical specifications. Compressed air generation and distribution system.	YES
16	Technical specifications. Process gases storage and distribution systems	YES
17	Functional specifications. Clean utilities generation, storage and distribution systems	YES
18	Procedure for installation of hygienic pipelines	YES
19	Natural gas distribution system- izometric	YES
20	Natural gas distribution system. Layout	YES
21	MTO – Ca	YES
22	MTO – PS	YES
23	MTO – PW	YES
24	MTO – TG	YES
25	MTO – WFI	YES
26	Purified Water distribution system. Isometric view - Level 1.	YES
27	Purified Water distribution system. Isometric view - Level 0.	YES
28	Water for iniection - hot - distribution system. Isometric view - Level 1.	YES
29	Water for iniection - hot - distribution system. Isometric view - Level 0.	YES
30	Water for iniection - cold - distribution system. Isometric view - Level 1.	YES
31	Water for iniection - cold - distribution system. Isometric view - Level 0.	YES
32	Pure steam distribution system. Isometric view - Level 1.	YES
33	Pure steam distribution system. Isometric view - Level 0.	YES
34	Floor plan – PW, WFI-H, WFI-CPS distribution system. Layout - Level 1.	YES
35	PW, WFI-H, WFI-C, PS distribution system. Layout - Level 0.	YES
36	Softened water distribution system. Isometric view - Level 1.	YES
37	Softened water distribution system. Isometric view - Level 0.	YES
38	Softened water distribution system. Layout - Level 1.	YES
39	Softened water distribution system. Layout - Level 0.	YES
40	Compressed air distribution system. Isometric view - Level 1.	YES
41	Compressed air distribution system. Isometric view - Level 0.	YES
42	Nitrogen distribution system. Isometric view - Level 1.	YES
43	Nitrogen distribution system. Isometric view - Level 0.	YES
44	Oxygen distribution system. Isometric view - Level 1.	YES
45	Oxygen distribution system. Isometric view - Level 0.	YES
46	Gases distribution system - CA, N2, Ar2, O2. Layout - Level 1.	YES
47	Gases distribution system - CA. N2, Ar2, O2. Layout - Level 0.	YES

ELECTRICAL & LOW CURRENTS		
1	Wiring diagram	YES
2	Electrical systems – general description	YES
3	Power balance	YES
4	List of internal power supply lines	YES
5	Calculations: electrical parameters	YES
6	Calculations: lighting system	YES
7	Catalogue cards for lighting fittings	YES
8	Catalogue cards for main electrical equipment	YES
9	Catalogue cards for main low-current devices	YES
10	MV switchgear – main, single-line diagram	YES
11	MV switchgear diagram – secondary circuits	YES
12	MV switchgear diagram – view and installation guidelines	YES
13	MV switchgear – specifications	YES
14	LV switchgear – single-line diagram	YES
15	LV switchgear diagram – control circuits	YES
16	LV switchgear diagram – view and installation guidelines	YES
17	LV switchgear – specifications	YES
18	LV distribution switchgear [R.xx] – single-line diagram [+ control circuits]	YES
19	LV distribution switchgear [MCC.xx] – single-line diagram [+ control circuits]	YES
20	LV distribution switchgear [RK.xx] – single-line diagram [+ control circuits]	YES
21	LV distribution switchgear [RO.xx] – single-line diagram [+ control circuits]	YES
22	LV distribution switchgear [RG.xx] – single-line diagram [+ control circuits]	YES
23	LV distribution switchgear [R.xx] – view	YES
24	LV distribution switchgear [MCC.xx] – view	YES
25	LV distribution switchgear [RK.xx] – view	YES
26	LV distribution switchgear [RO.xx] – view	YES
27	LV distribution switchgear [RG.xx] – view	YES
28	LV distribution switchgear [R.xx] – product order form	YES
29	LV distribution switchgear [MCC.xx] – product order form	YES
30	LV distribution switchgear [RK.xx] – product order form	YES
31	LV distribution switchgear [RO.xx] – product order form	YES
32	LV distribution switchgear [RG.xx] – product order form	YES
33	Central battery system – diagram	YES
34	Central battery system – specifications	YES
35	SSP system – diagram	YES
36	SSP system – diagram	YES
37	Access control system – diagram	YES
38	Access control system – diagram	YES
39	Intruder and burglar alarm system – diagram	YES
40	Intruder and burglar alarm system – diagram	YES
41	CCTV system – diagram	YES
42	CCTV system – diagram	YES
43	Gas detection system – diagram	YES
44	Gas detection system – diagram	YES
45	Smoke extraction system – diagram	YES
46	Smoke extraction system – diagram	YES
47	Structured cabling system – diagram [+ layout of IT cabinets]	YES
48	Structured cabling system – diagram [+ layout of IT cabinets]	YES
49	General lighting – projections [each level]	YES
50	Escape route lighting – projections [each level]	YES
51	Sockets and three-phase power system – projections [each level]	YES

52	Cable trays – projections of electrical and low-current systems [each level]	YES
53	Internal power supply line routes and electrical switchgears – projections [each level]	YES
54	Equipotential bonding system – projections [each level]	YES
55	Building code guidelines – projections [each level]	YES
56	SSP system – projections [each level]	YES
57	Access control system – projections [each level]	YES
58	Intruder and burglar alarm system – projections [each level]	YES
59	CCTV system – projections [each level]	YES
60	Gas detection system – projections [each level]	YES
61	Smoke extraction system – projections [each level]	YES
62	Structured cabling system – projections [each level]	YES
63	3D model: detailed view of LOD 300 components. The model should include lighting, sockets, trays, SSP detectors, switchgear, CCTV cameras, access control equipment, intruder and burglar alarm equipment, equipotential bonding connections (rails), building code guidelines (faults), gas detection equipment, smoke extraction equipment, sockets and IT cabinets.	YES

AUTOMATION		
1	Table of automation points	YES
2	Technical description (PL)	YES
3	Leakage controller	YES
4	LDS components arrangement	YES
5	Diagram of a LDS	YES
6	Eight zone sensory cable	YES
7	One zone sensory cable	YES
8	One-zone sensory tape	YES
9	Point sensor for leakage detection	YES
10	Autocouplers	YES
11	Multi-zone leakage control panel	YES
12	Table of automation points	YES
13	Controller of the gas	YES
14	Technical description	YES
15	Arrangement of elements	YES
16	Diagram Building	YES
17	Oldham MX43 controller	YES
18	Oldham gas detector	YES
19	Buffer power supply PSBS	YES
20	Signal Tower Half Dome 9	YES
21	Automation Systems Airlocks (PL)	YES
22	Airlock panel schematic	YES
23	IO island schedules	YES
24	Table of automatic control points	YES
25	BAS description	YES
26	Layout of BAS components	YES
27	Monitoring – automatic control – BAS	YES
28	Routes – automatic control – BAS	YES
29	Control cabinet BAS1	YES
30	ark 1_Scope of automatic control in the system	YES
31	Title: Scope of automatic control in the system	YES
32	ark 1 Automation of comfort in office	YES
33	ark 1 Monitoring and measurements	YES
34	Title: Monitoring and measurements	YES
35	Power supply and control box for fan coils	YES
36	P&ID diagrams of laboratory and production areas	YES
37	Relay boxes for fan coil control	YES
38	Control cabinet BAS1_	YES
39	Power supply and control box for fan coils	YES
40	Indoor temperature controller	YES
41	Installation accessories for controller RDF302	YES
42	Referencing unit and indoor controller	YES
43	Controller for fan coils with communication	YES
44	Housing of Mini Pragma automation board	YES
45	Hermetic junction box housing	YES
46	HVAC automation systems	YES
47	AHU – points	YES
48	MAHU – points	YES
49	Location of HVAC components	YES
50	HVAC – block diagram of automation ark 1	YES
51	Air handling unit	YES
52	P&ID diagrams of the ventilation system in individual rooms and areas	YES
53	Cabinet – IC_HVAC1	YES
54	Air handling unit	YES
55	EMS monitoring island cabinet	YES
56	EMS_List of panel computers	YES
57	Environment Monitoring System (EMS)	YES
58	Location of EMS elements	YES
59	Cabinet location	YES
60	Cabinet with pressure transducers	YES
61	EMS monitoring system in ZFP buildings	YES
62	Cabinet with a 9-inch EMS control panel	YES
63	EMS industrial computer panel	YES

64	SIMATIC PCS7 CPU 410-5H (6ES74105HX080AB0) controllers	YES
65	Dispersed I-O_SIMATIC ET 200SP. Brochure	YES
66	Dispersed I-O_SIMATIC system interface module	YES
67	Analog inputs module SIMATIC ET200SP_AI_	YES
68	Serial communication module SIMATIC ET200SP	YES
69	Pressure transducer, DS1 series	YES
70	Indoor temperature and humidity sensor QFA3171	YES
71	Indoor temperature sensor QAC3171	YES
72	Pharmaceutical temperature sensor, TOPPS series	YES
73	Temperature and flow rate transducer	YES
74	Dew point transducer FA510	YES
75	Desktop airborne particle counter IsoAir310P	YES
76	22” industrial computer SIMATIC ITC2200	YES
77	9” control panel SIMATIC HMI KTP900 BASIC	YES
78	Automation Systems Heating Station	YES
79	xr heating station components arrangement	YES
80	Heating substation automation – +R-HWPS	YES
81	P&ID diagram P& ID of heating substation – I/O – HWPS	YES
82	Power engineering system monitoring automation	YES
83	Table of automatic control points	YES
84	Location of PMS automatic control components	YES
85	ark 1 PMS cable routes	YES
86	PMS- block diagram of automation	YES
87	Automation Systems Cooling Station	YES
88	Xr cooling station components	YES
89	Cooling substation automation (distribution) – +R-CWPS	YES
90	P&ID diagram of the cold distribution substation – I/O-CWPS	YES
91	BMS.GMP_F I+II	YES
92	BMS.nGMP_F I+II	YES
93	BUILDING MANAGEMENT SYSTEM	YES
94	BMS architecture. Flowchart	YES

PROCESS		
1	Room list	YES
2	Process and Utillities Equipment List	YES
3	Lab Equipment List	YES
4	Material Flow Lay-Out 1 ground floor	YES
5	Material Flow Lay-Out 2 ground floor	YES
6	Material Flow Lay-Out 2 - controlled material - ground floor	YES
7	Personnel flow Lay-Out - ground floor	YES
8	Personnel flow Lay-Out - first floor	YES
9	Personnel flow Lay-Out - second floor	YES
10	User point Lay-Out (for each level and all services) -ground floor	YES
11	User point Lay-Out (for each level and all services) - first floor	YES
12	Pure fluids PFDs and technical utilties PFDs	YES
13	Fluid Consumption List (summary and detailed user by user) with definition of assumptions	YES
14	Fluid List	YES
15	Process Equipment URS (new URS for filling line for syringes, vials and cartrdges + 5 URS for microbiological lab)	YES
16	HAZOP	YES
17	ATEX	YES
18	CIP system distribution diagram	NO
19	CIP system distribution diagram – isometric view	NO
20	SIP system distribution diagram	NO
21	SIP system distribution diagram – isometric view	NO

Overview of the list of User Requirements Specifications (URS) required to be developed and approved as part of the baseline design

1. Primary User Requirements Specifications (URS)

Document containing a set of requirements for the building, all areas included in the baseline design, critical auxiliary systems (HVAC, LAF, PW, WFI, process gases, i.e. compressed air, nitrogen), main computerized systems being developed as part of the project (i.e. RMS, BMS, PMS) and main corporate computerized systems to be rolled out at subsequent stages of the project.

2. User Requirements Specifications (URS) for processing equipment:

- Weighing/sample collection chamber
- System for safe transport and weighing of substances (isolator)
- Solution preparation system
- Disposable (single-use) solution preparation tanks/set-ups/systems
- Autoclave
- Decontamination shower
- Filling line
- Automatic washer

3. User Requirements Specifications (URS) for laboratory equipment:

- Five User Requirements Specifications (URS) for individual devices installed in the area of the Microbiological Laboratory (including the isolator).