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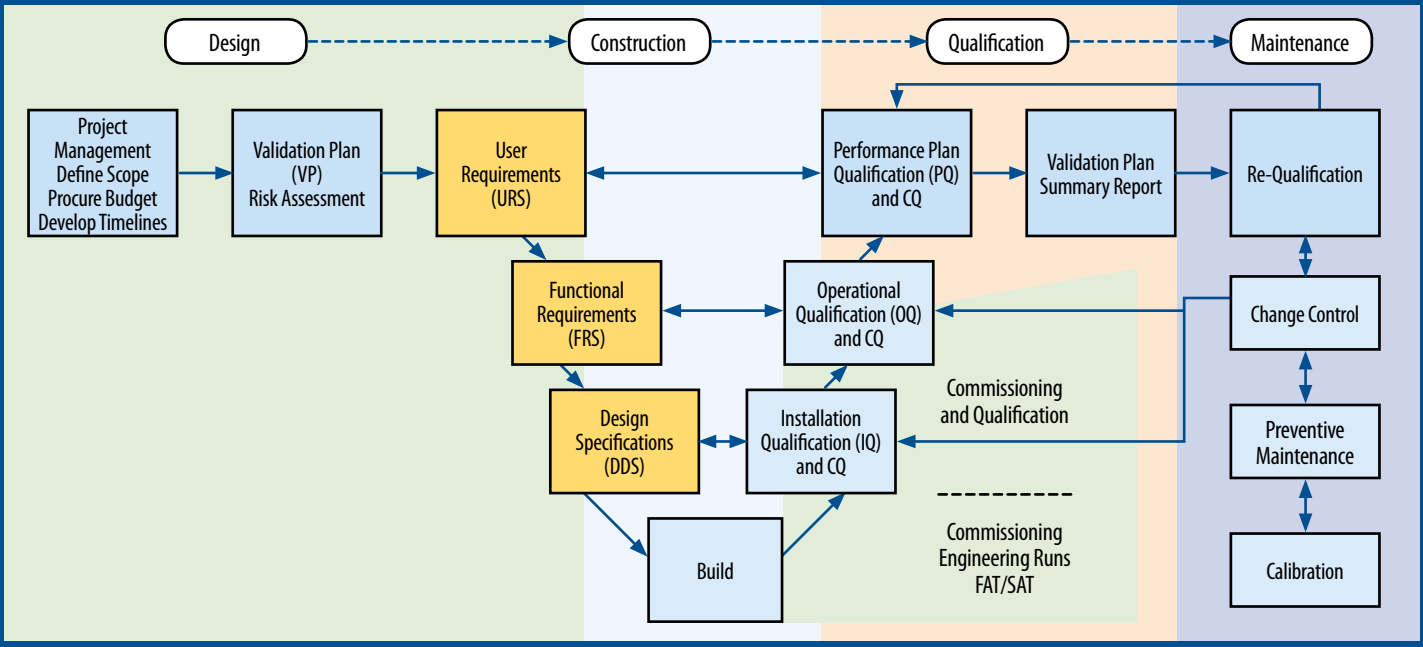
Cleanrooms

– expertise you can rely on



The ISPE general V-model

Cleanrooms

Elomatic has over 30 years' experience in completing demanding cleanroom projects both domestically and abroad. Our experience covers all project kinds, sizes and their phases (CD, BD, DD, DR, DQ, C, IQ and OQ). Our intimate knowledge of processes and their GMP requirements make us the ideal partner for working cleanroom solutions.

In order to achieve Good Manufacturing Practice (GMP) cleanrooms, Elomatic applies the Society for Pharmaceutical Engineering's (ISPE) guidelines, unless otherwise required by the client. We are thoroughly familiar with GMP regulations such as EU, FDA and WHO cGMP.

For particle-based cleanliness, we mostly follow the ISO 14644 standard. Elomatic`s cleanroom designers and project management normally concentrate on the first five parts of the standard. If the clients so desires, other standards can also be followed.

Cleanroom expertise you can rely on

The first five parts of the ISO 14644 standard family are of importance for cleanroom designers.

EN-ISO 14644-1	Classification of Air Cleanliness
EN-ISO 14644-2	Specifications for Testing and Monitoring to Prove Continued Compliance with ISO 14644-1
EN-ISO 14644-3	Test Methods
EN-ISO 14644-4	Design, construction and start-up
EN-ISO 14644-5	Operations
EN-ISO 14644-16	Code of practice for improving energy efficiency in cleanrooms and clean air devices (new standard part)

ISPE tools and V-model

At Elomatic we make extensive use of tools provided by ISPE to facilitate a clearer understanding of the application of different GMP regulations, standards and guidelines to find suitable solutions to GMP challenges.

By combining ISPE's excellent source of reference information with our practical experience we are able to solve most clients' GMP related questions. Local laws and codes are naturally applied.

Once a cleanroom project is started, we adhere to the ISPE general V-model in all projects, unless otherwise required. Every phase is approved and completed with documented confirmation before proceeding to the next phase. It all starts from the user requirements and ends with the very same user requirements.

User requirements – URS

The URS is arguably the most important document in the whole GMP project, as it defines all the users' GMP critical demands for the process, clean utilities, cleanrooms, cleanroom HVAC and black utility. URS in the GMP context means a documented definition of the key requirements stated by the user.

Elomatic can assist customers to draw up user requirements, if necessary. It is critical that the URS states what GMP regulations should be followed and what cleanliness grades are required. EU GMP and FDA cGMP requirements are the two mostly referred to by our clients, but also WHO, Japanese, Brazilian, Chinese, Indian, Mexican or other regulations can be used, if required.

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Cleanroom layout

Layout design should only be started once a clear understanding of the user requirements has been gained. In the first step Elomatic`s and the client`s experts consider what layout is feasible with consideration for basic rules.

- Airlocks and pressure cascading regimes
- US and EU cleanliness grades, in particular with regard sterile drugs produced in aseptic processing.

The crucial role of HVAC

HVAC design is an extremely important part of a cleanroom project. Our experts have vast experience in ensuring that HVAC systems produce the desired conditions for production. HVAC systems also commonly represent large operating costs.

An extremely important factor is whether recirculated air or outside air is used in ventilation to best satisfy URS requirements. At Elomatic, we prefer to use recirculated air in a cleanroom ventilation system, if it is not prohibited for any reason, thereby reducing energy consumption and CO_2 emissions. Energy efficiency and environmental effects are thorougly evaluated.

Direct and indirect impact systems

It is of critical importance to determine whether the HVAC or utility system has a direct or indirect impact on the product.

Direct impact systems are designed and commissioned in line with GEP and are also subject to qualification practices that incorporate enhanced review, control, and testing against specifications or other requirements necessary for cGMP compliance.

Critical Parameters

- **Critical Attribute**: A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality (ICH Q8(R2))
- **Critical Process Parameter**: A process parameter whose variability has an impact on a critical quality attribute and therefore should be monitored or controlled to ensure the process produces the desired quality (ICH Q8(R2))
- **Critical Parameter (in HVAC)**: A room variable (such as temperature, humidity, air changes, room pressure, particulates, viable organisms, etc.) that, by law or by determination from pharmaceutical product development data, affects product strength, identity, safety, purity, or quality (SISPQ)
- **Acceptance Criterion**: The predetermined result of a special test. In HVAC, the upper and lower limits of the room environment (critical parameters). If these limits are exceeded, the exposed pharmaceutical product may be considered adulterated.

Indirect systems are designed and commissioned following GEP alone. Indirect impact systems can affect the performance or operation of a direct impact system.

Once the impact type of the system has been determined, the appropriate commissioning and validation activities can be applied.

Critical parameters

The critical parameters for products manufactured in a cleanroom environment need to be specified in the URS. Elomatic's designers are thoroughly competent in gathering all the necessary information as per the ISPE guideline.

- Critical Attributes
- Critical Process Parameters
- Critical Parameter (in HVAC)
- Acceptance Criteria

Validation of cleanrooms and cleanroom HVAC

The first validation activity in cleanroom and cleanroom HVAC projects is the DQ, whereas the last is the approval of all the required design documents. When everything is complete, a design qualification (DQ) report is drawn up and signed. It is a generally applied approach that construction work cannot be started before design qualification is done.

The next step is construction, which is followed by commissioning (C), installation qualification (IQ), operational qualification (OQ) and finally performance qualification (PQ). Each has to be approved before the next step can start and approval of all steps has to be documented.

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Infusion solution factory, Turkmenistan


Orion


Turkmenistan

Selected References

FinVector, Kuopio, Finland (2017)
Detail design, black utility systems and clean utility systems (BSL2 facility)
- Cleanroom area of 700 m^2 in EU GMP Vol. 4 Annex 1 grades D and C

Fit Biotech, Tampere, Finland
Conceptual design for a vaccine plant, from fermentation to fill & finish.
- Cleanroom area of 214 m^2 in EU GMP Vol. 4 Annex 1 grades D, C and B

FinVector, GMP4/BSL2, Kuopio, Finland (2016)
Basic Design, Black Utilities, Clean utilities, WFI, PS, process calculations (BSL2 facility)
- Cleanroom area of 700 m^2 in EU GMP Vol. 4 Annex 1 grades D and C

PCAS, Turku, Finland
CD for upgrading room conditions and adding PAL/MALs for existing API production
- Cleanroom area of 30 m^2 in EU GMP Vol. 4 Annex 1 grade D

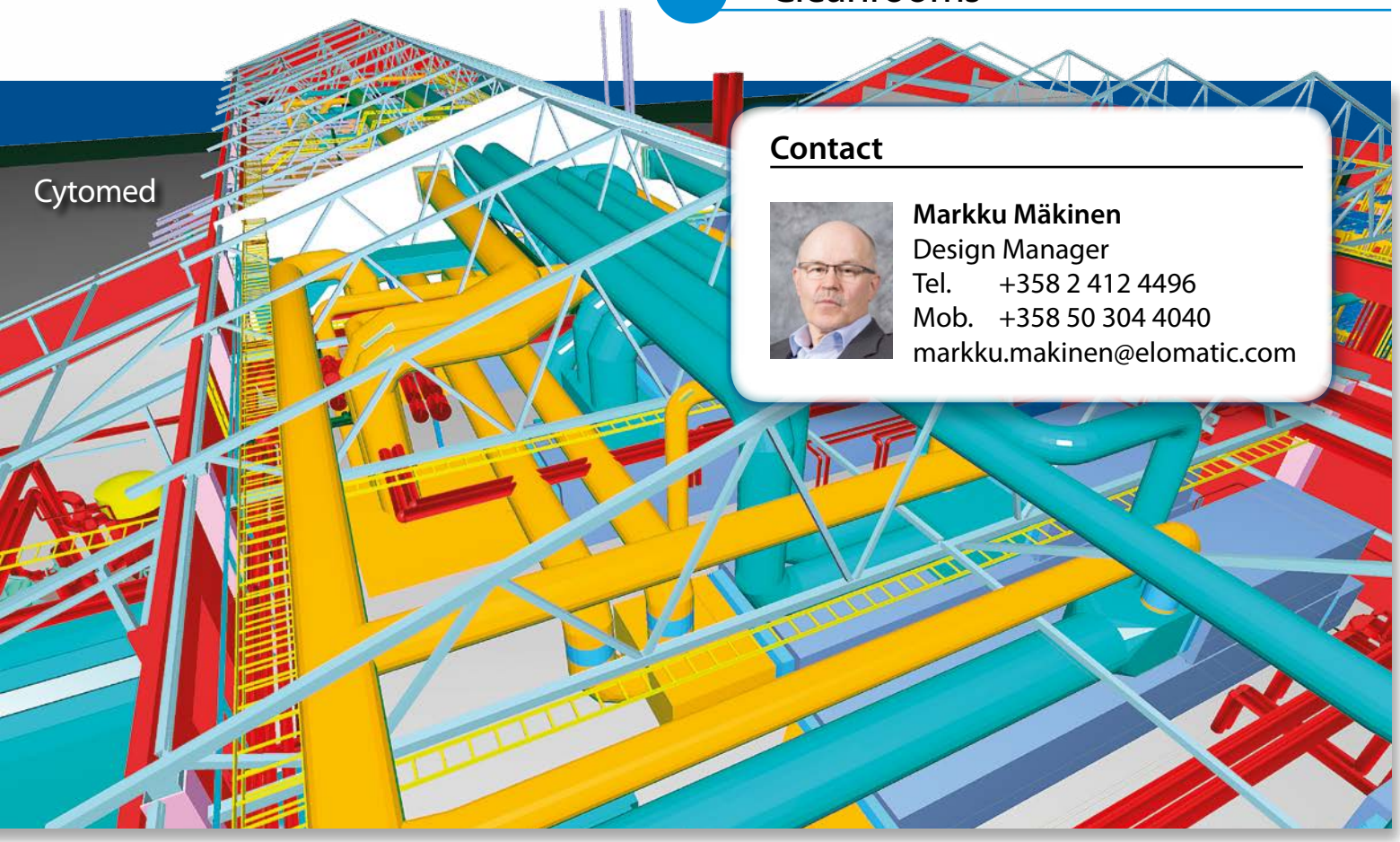
Shahid Ghazi Pharmaceutical Co, Tabriz, Iran
Conceptual engineering for 3 x LVP and 1 x SVP production lines including laboratories, warehouse, black & clean utilities and common dispensing area (greenfield)
- Cleanroom area of 2600 m^2 in EU GMP Vol. 4 Annex 1 grades D, C and B

PerkinElmer, Turku, Finland (2012–2016)
Complete renovation of Diagnostic reagent production cleanroom HVAC, simultaneously with on-going production (executed in four phases)
- Cleanroom area of 3000 m^2 in EU GMP Vol. 4 Annex 1 grade D and internal grade E.

FinVector, Kuopio, Finland (2015)
Conceptual Design, GMP4 production expansion (BSL2 facility)
- Cleanroom area of 700 m^2 in EU GMP Vol. 4 Annex 1 grades D and C

Turku University Hospital, Finland
GMP consultation and HVAC design for expansion of a radiopharmaceutical laboratory in PET center

Cleanrooms



Contact

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- Cleanroom area of 60 m^2 in EU GMP Vol. 4 Annex 1 grades D and C

NovaMedica, Moscow, Russia (2014)

Conceptual design of a new pilot laboratory for clinical research and product development

- Cleanroom area of 30 m^2 in EU GMP Vol. 4 Annex 1 grades D and C

NovaMedica, Moscow, Russia

Conceptual design of a new pharmaceutical factory site for small volume IV solutions

- Cleanroom area of 1030 m^2 in EU GMP Vol. 4 Annex 1 grades D, C and B

GAPInsaat A.S, Turkmenistan, Ashgabat

Conceptual design of a new factory for manufacturing of pharmaceuticals from licorice plant roots

- Cleanroom area of 590 m^2 in EU GMP Vol. 4 Annex 1 grades D, C and B

Cytomed, St Petersburg, Russia

Basic design of a new production facility for several dosage forms and biological and chemical APIs

- Cleanroom area of 1130 m^2 in EU GMP Vol. 4 Annex 1 grades D, C and B

Ministry of Health and Medical Industry, Ashgabat, Turkmenistan (2012–2013)

Turnkey delivery of an infusion production process, including equipment, cleanrooms and clean room HVAC, piping, E&IC, site supervision, start-up and validations

- Cleanroom area of 400 m^2 in EU GMP Vol. 4 Annex 1 grades D and C

Orion Oyj, Turku, Finland (2012)

Detail design of HVAC, black and clean utility systems and site supervision for hormone gel expansion in total area of 6000 m^2

- Cleanroom area of 2000 m^2 in internal grades E, F and G

Novo Nordisk, Denmark

Conceptual design of a fill finish factory.

- Cleanroom area of 800 m^2 in EU GMP Vol. 4 Annex 1grades D, C and B.

Cytomed, St Petersburg, Russia

Conceptual design of a new production facility for several dosage forms and biological and chemical APIs

- Cleanroom area of 1130 m^2 in EU GMP Vol. 4 Annex 1 grades D, C and B

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Elomatic is a leading European consulting and engineering company. Our close to 900 professionals work in machinery and equipment manufacturing, pharmaceutical, process, energy, offshore and marine industry projects.

We offer consulting, engineering, product development and project management services as well as products and turnkey solutions to industrial and public sector customers.

The cornerstones of our success are customers that are leaders in their respective fields and professional, customer-oriented and motivated personnel.

- Technical Consulting
- Engineering
- Project Management
- Product and Service Development
- Products & Turnkey Solutions
- Software Development
- Design Software Solutions

Key customer segments

- Pharmaceuticals
- Process Industries
- Energy
- Foodstuffs industry
- Starch and Potato Processing
- Machinery and Equipment Manufacturing
- Marine & Offshore
- Oil & Gas

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We operate globally and have clients in over 80 countries. Our offices are located in Finland, China, India, Italy, the Netherlands, Poland, Serbia, Russia and the UAE.

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