Aseptic preparations, including TPN, for a limited number of patients

Group F

Objective

Presentation of our business case:|

setting up an aseptic TPN production
in the “Hilton Pharmacy”

instead of a TPN preparation on the wards

SMF
Site Master File

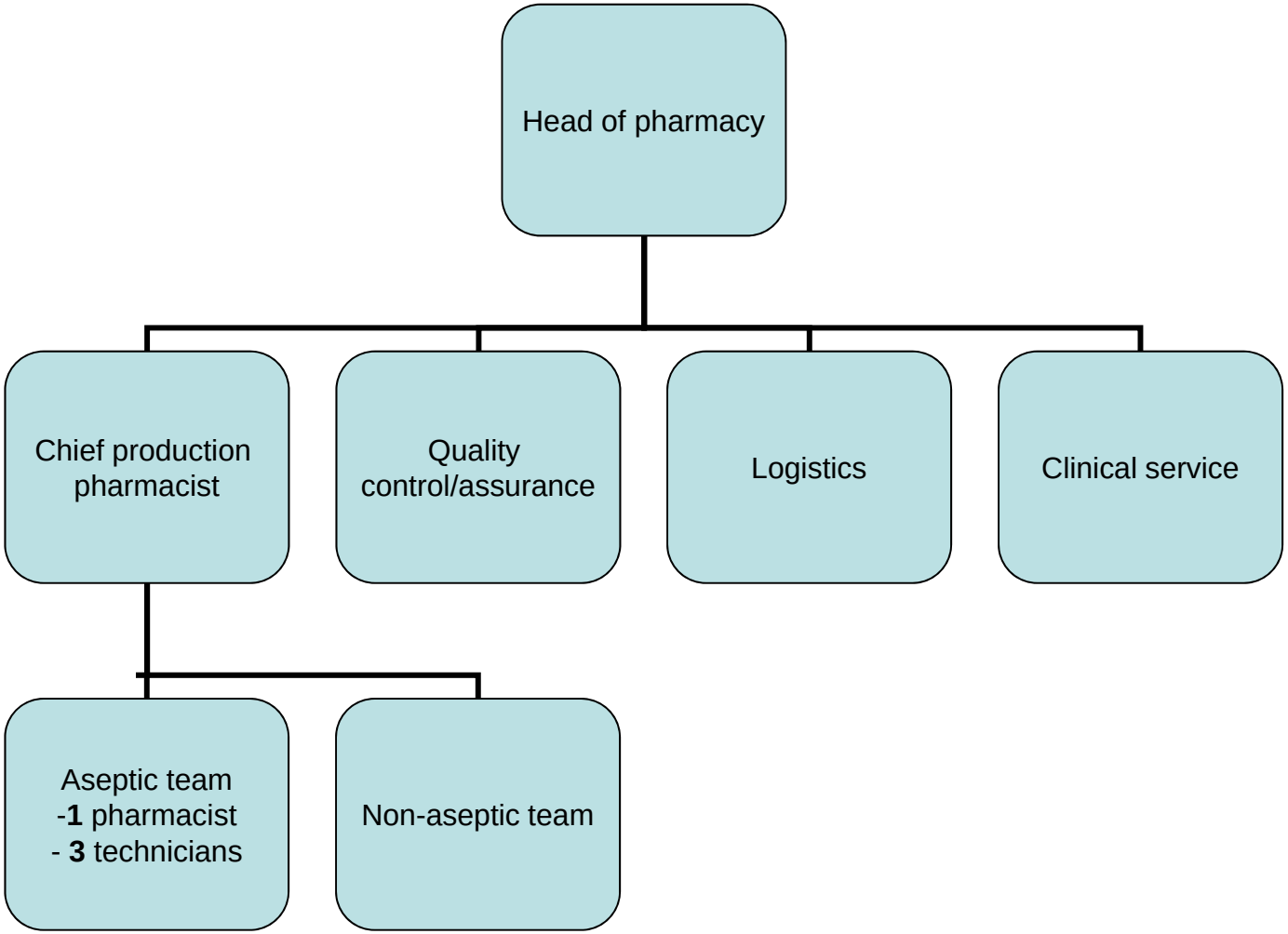
Mission

- We prepare safe, high quality, ready to use medication to address individual patients' needs at the right time.

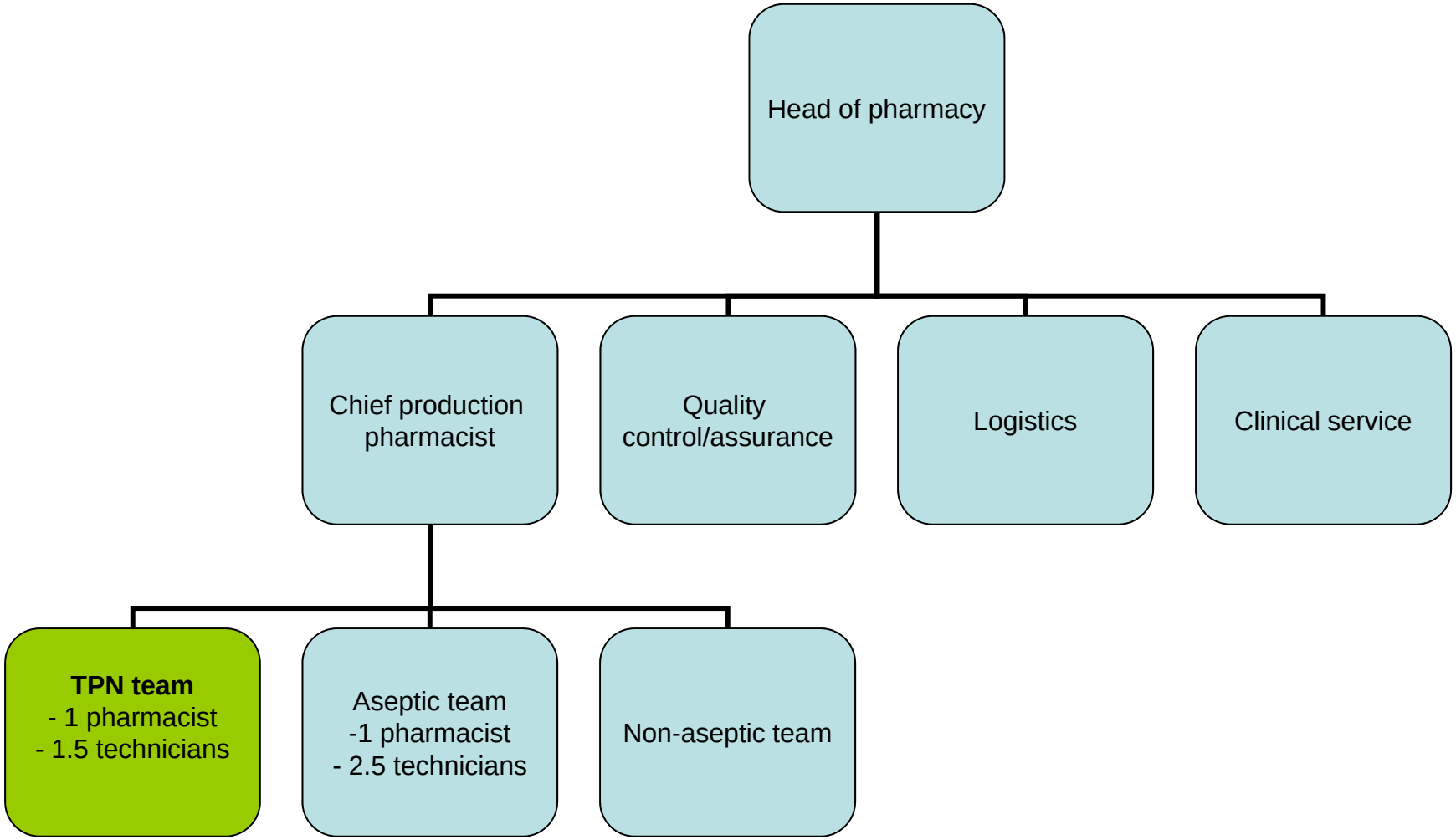
Strategy

- We develop our services in collaboration with the physicians with the focus on ongoing patient safety.
- We employ well trained staff and produce according to the best preparation practice and in a cost effective process.
- We guarantee the in time delivery of our products.

Actual Organogram



New Organogram



Product lines

TPN Team

- Individual TPN for neonate ICU
  7000 bags / year (15-25 bags a day)
  Batch size: daily production and on Friday for the weekend
  stability (3 to 8 days)

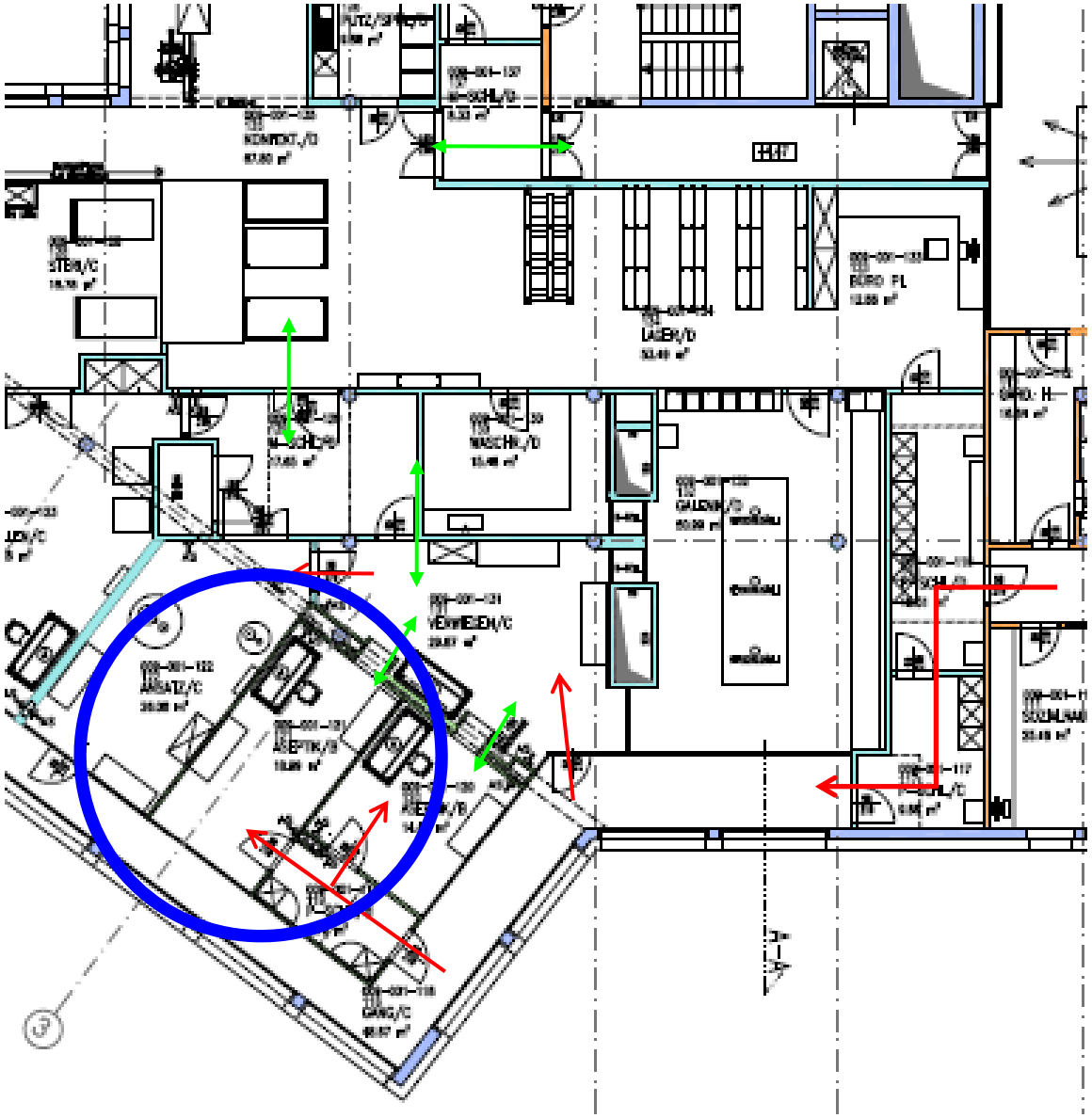
Aseptic Team

- syringes
  Intravitreal injections
- iv infusion bags
  Bupi/Fenta
  Antibiotics
- infusion pumps (for home care)

Technical infrastructure

- Cleanroom grade B
  (because we plan for the future: for an existing cleanroom a lesser grade may be applicable according to the PIC/S PE010)
- LF cabinet for TPN
- TPN machine Baxa compounder
- Scales
- Refrigerator

- Incubator for microbiological monitoring
- Aseptic filling: repeater pump



Floor plan

100 m^2 for aseptic preparation

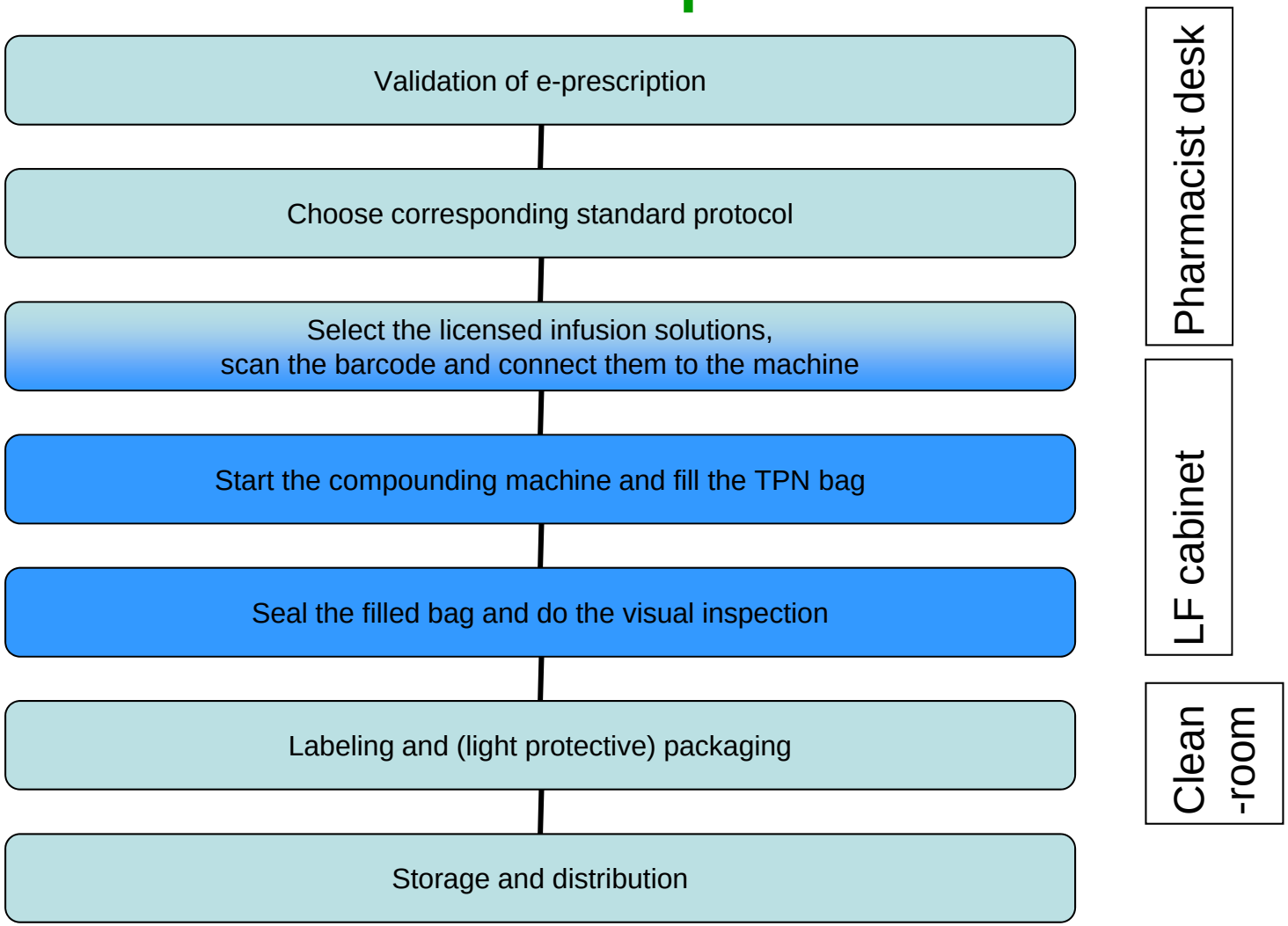
2 LF cabinets
in cleanroom grade B

Personnel

Material

Group F – aseptic preparations (TPN)

Production process



Business Plan
(Executive summary)

Business Plan

- Current situation
  individual TPN not commercially available
  neonate TPN preparation on the ward:
  high patient risk
- Proposal for updating of the current facility
- Trend in therapy:
  increasing demand of individual TPN

Costs and Benefits

Specification	**Annual sum** (€)
Salary	-102 600
Gowns, single use devices	-10 000
Room maintenance	-62 000
External lab	-10 000
Amortisation of equipment (5 y)	-50 000
	-234 600
Income, €35/TPN	+262 500
Profit	**+ 27 900**

Product design

Product development

Life cycle

Needs:

- no product commercially available, as is has to be individualized to the patient: this need cannot be fulfilled by industry
- short shelf-life of ready to use admixtures (with trace elements and vitamins)
- sometimes daily change of composition

Product development

Policy

patient safety first!

- no compounding of TPN on the ward by nurses, because of the high microbiological contamination risk
- compatibility testing sometimes required
- high flexibility
- for TPN: electronic prescription according to a standardized protocol (step-up protocol for nutrition)

Product development

Pharmaceutical development

- espghan guidelines (guidelines regarding the composition of TPN)
- information from the pharmaceutical manufacturer of the solution
- mixing components in a predefined sequence (information by manufacturer of automated pump)
- stability: degradation of vitamins, therefore short shelf-life of max. 3 days (flexibility and quality are guaranteed)

Biopharmaceutical aspects

- Solubility of Calcium combined with Phosphate has to be assessed (use of glycerophosphate)
- Emulsion stability (in neonate TPN the lipid is given separately, so there is less problem)
- Stability of vitamins has to be assessed

Packing materials

- EVA bags for TPN
  eg Freka ® bag
  medical device CE
- Type sample for conformity test (no certificate)
- Product information sheet
- try to have a contract regarding information about changes and uniform quality

Packing material

Specifications for batch testing:

- visual analysis in comparison to the type sample
- Batch No and Exp Date
- CE Label

Quality management

Quality Management

- Risk analysis
- VMP (equipment and process)
- Quality control
- Monitoring
- Auditing

not addressed:

- Change control
- Documentation

Patient risk in the production process

- Prescription
- Calculation
- Selection of components
- Preparation
  stability / degradation
  contamination
- Distribution and storage
- Administration and adverse effects

Risk analysis – TPN production

Parameter	**Risk**	**Harm**	**S**ev erit y	**O**ccur rence	**D**et ecti on	**R**isk	**Measure**
Admixture	Wrong raw material	death	5	1	5	25	Bar coding
Contamination of TPN	Missing hygiene measures	infection	4	2	3	24	Monitoring training
LF bench	Air flow not sufficient	Microbial contamination	4	1	1	4	Alarm of LF Particle monitoring
Medical devices	Bad quality (eg contamination)	death	5	1	5	25	Purchase from qualified suppliers
Distribution / storage	Etc.						

Risk analysis

Risk acceptance

- All possible measures are taken to minimize the risks
- For the preparation of TPN for neonates the remaining risks have to be accepted, as the lack of TPN is worse

Validation Master Plan

Validation activities

- Cleaning procedures
- GMP-relevant equipment
- GMP-relevant processes

Training

- aseptical handling
- basic GMP-training

Validation Master Plan

Documentation

- Every validation has a unique number
- Validation protocols and reports have to be approved by production and QA
- List of equipment and processes with validation status

Validation Master Plan

Equipment and processes	GMP-relevant	Val. No	Status
Cleanroom	yes	V01	Yearly revalidation
LF cabinet	yes	V02	Yearly revalidation
TPN machine	yes	V03	Planned
Scales	yes	V04	done
Incubator (monitoring)	yes	V05	Work in progress
Refrigerator	Yes	V06	Planned
TPN preparation (aseptic filling)	Yes	V07	Yearly revalidation

Quality control

QC facility needed:

- microbiological laboratory
- 2nd lab: eg for validation of formulations: Coulter counter (lipid emulsion stability) particle control (visible particles)

- Raw material: na, as only licensed medicines are used

Monitoring

environmental monitoring (particles, microbiological contamination)

- particle counting in LFC during production
- active air sampling in the cleanroom
- settle plates in LFC
- glove monitoring of staff
- media fill (at the end of every production day)

Personnel Validation

- Media fill prior to aseptic preparations
  3x 10 media fills
- biannual revalidation with 10 media fills (in addition to the daily media fills for monitoring)

Auditing system

external lab (sterility testing, identification of possible microbiological contamination)

- auditing of the external lab
- contract defining responsibility
  QS system (GMP certificate, ISO)
  OOS / deviation management
  validation of methods

Auditing system

Internal lab:

- QA does yearly internal audits
- audits by an external professional every 3 years

Thank you for your attention

buy TPN at the Hilton Pharmacy