Setting Up A Serum Eye Drops Program

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This presentation shares our experience on how to use the synergies of being a blood and tissue bank when starting a serum eye drops (SED) program

Though the process might not be familar to eye bankers, it is strongly related to eye banks and their end users

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Red Cross Blood Transfusion Service of Upper Austria runs a blood and tissue bank with more than 50.000 blood and 500 tissue donations, mainly serving the federal state of Upper Austria.

- Three different blood products (erythrocytes, thrombocytes, plasma)
- Two classical medicinal products (one investigational medicinal product and serum eye drops)
- Eight different autologous and allogeneic tissues and cells (cornea, DMEK, sclera, heart valves, amniotic membrane, cranial bone, ovarian tissue, peripheral blood stem cells)

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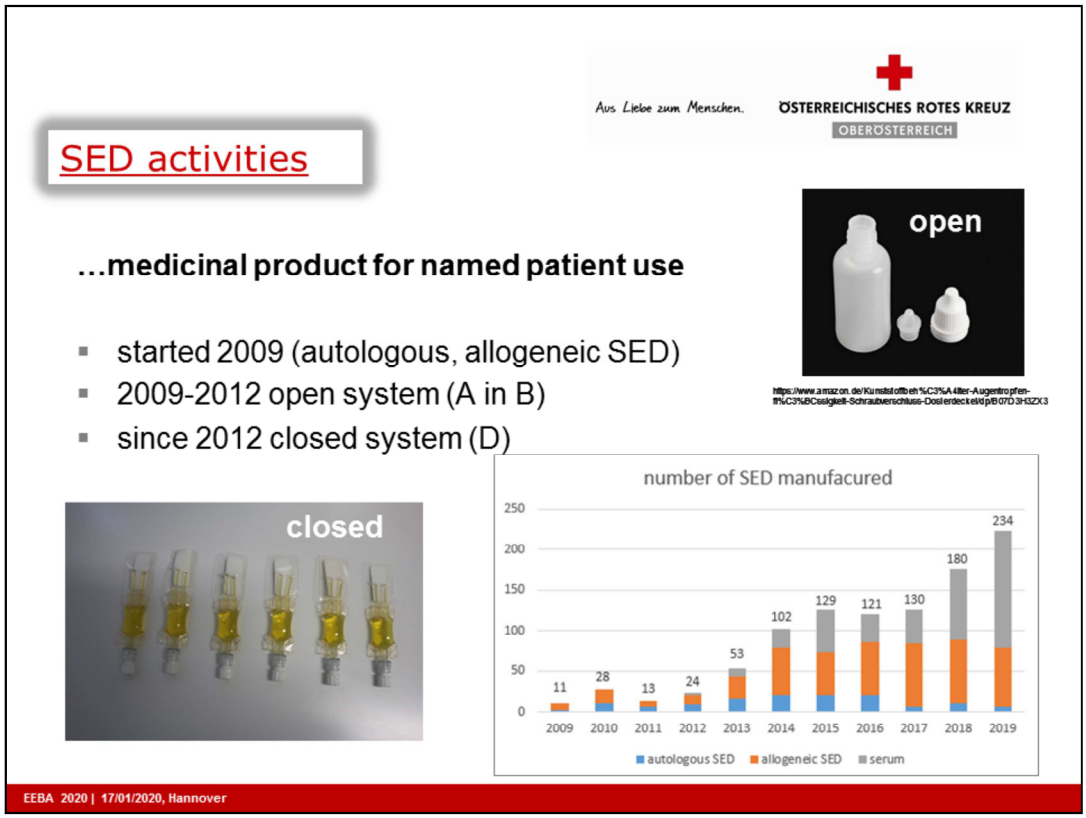

- Our serum eye drops program started on request of some of our cooperating ophthalmologists of our eye bank in 2009.
- SED are classified as classical medicinal products in AT.
- Named patient use only way to overcome required registration of medicinal product
- Until 2012 both autologous and allogeneic SED processed with open system (filling performed in laminar air flow class A with B-background)
- Since 2012 closed SED processing system from company „Meise Medizintechnik“ in use → transfer of processing to clean room class D
- Steadily growing number of serum units and patients within the last decade (in 2019 processing of 234 serum donations)

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SYNERGIES	BLOOD BANK REQUIREMENTS	TISSUE BANK REQUIREMENTS	ADDITIONAL REQUIREMENTS
Blood donor evaluation	X	-	-
Blood donor procurement	X	-	-
Blood donor testing	X	-	-
QMS	X	X	-
Premises	X	X	-
Processing in clean room	X (grade D)	X (grade D, C, B)	-
Storage	X (-30°C up to room temperature)	X (LN-tanks up to 31°C)	-
ISBT128 coding	X	X	-
QC	X (infectious diseases, sterility, cell couting)	X (infectious diseases, sterility, cell couting)	Stability program
Distribution	X	X	Via pharmacy
Traceability	X	X	-
Vigilance	X	X	-
Clinical application	-	Ophthalmologists	Prescription (named-patient use)
Release	X	X	Head of Production Head of Quality Control Qualified Person
Retention samples	X	X	also for consumables and reagents

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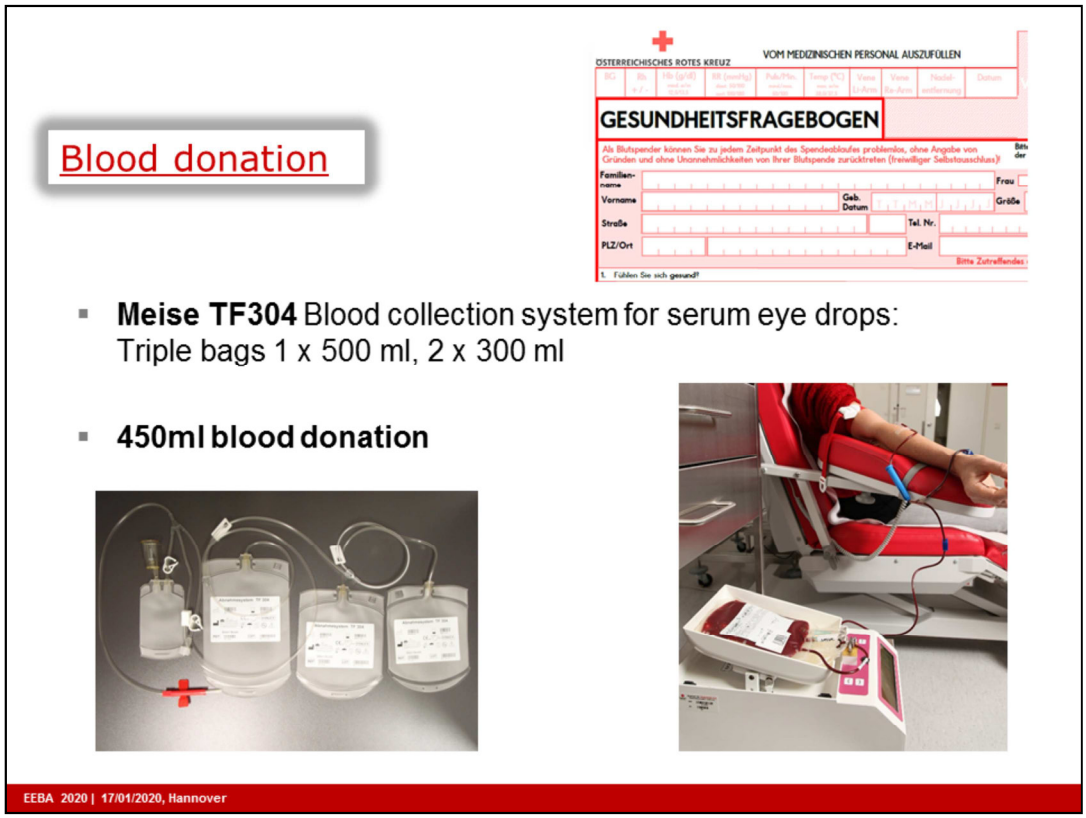
When implementing SED program, synergies of being a blood and tissue bank could be perfectly used.

What could blood and tissue activities offer to fulfill medicinal product requirements?

1) Blood donation and testing is already in place.
2) Benefit from already existing quality management system, premises as well as knowledge about processing storage, coding distribution traceability vigilance, quality control and release

What needs to be established additionally?

1) Set up of stability program for SED
2) Distribution of SED via pharmacy
3) Named-patient use prescription by ophthalmologist
4) Three legal functions need to be implemented (Head of Production, Head of Quality Control, Qualified Person)



If all requirements for whole blood donation, as given in blood directives, are fulfilled, 450 mL whole blood with TF304 system without any anticoagulant can be withdrawn.

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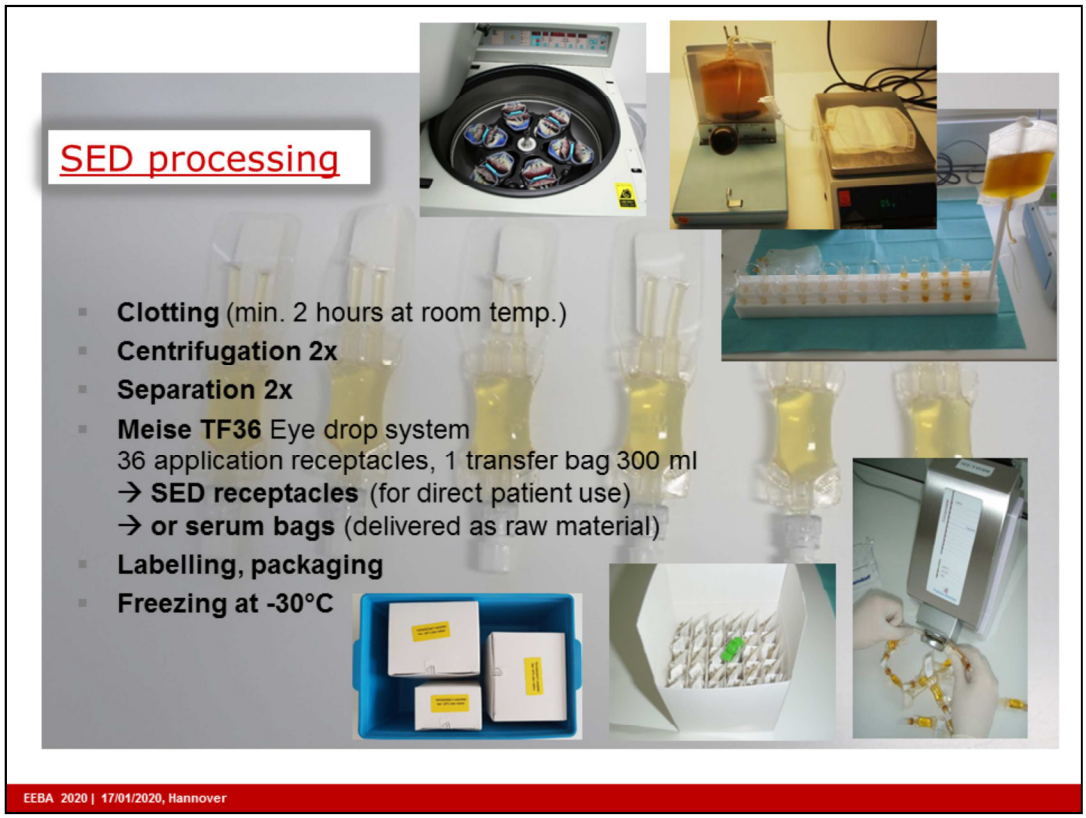

Blood clotting is awaited for at lease two hours at room temperature. Blood bag is centrifuged and separated twice.

Then, obtained serum is either aliquoted to SED receptacles in closed TF36 system or kept in transfer bag and stored as serum raw material for another blood bank, which processes diluted SED.

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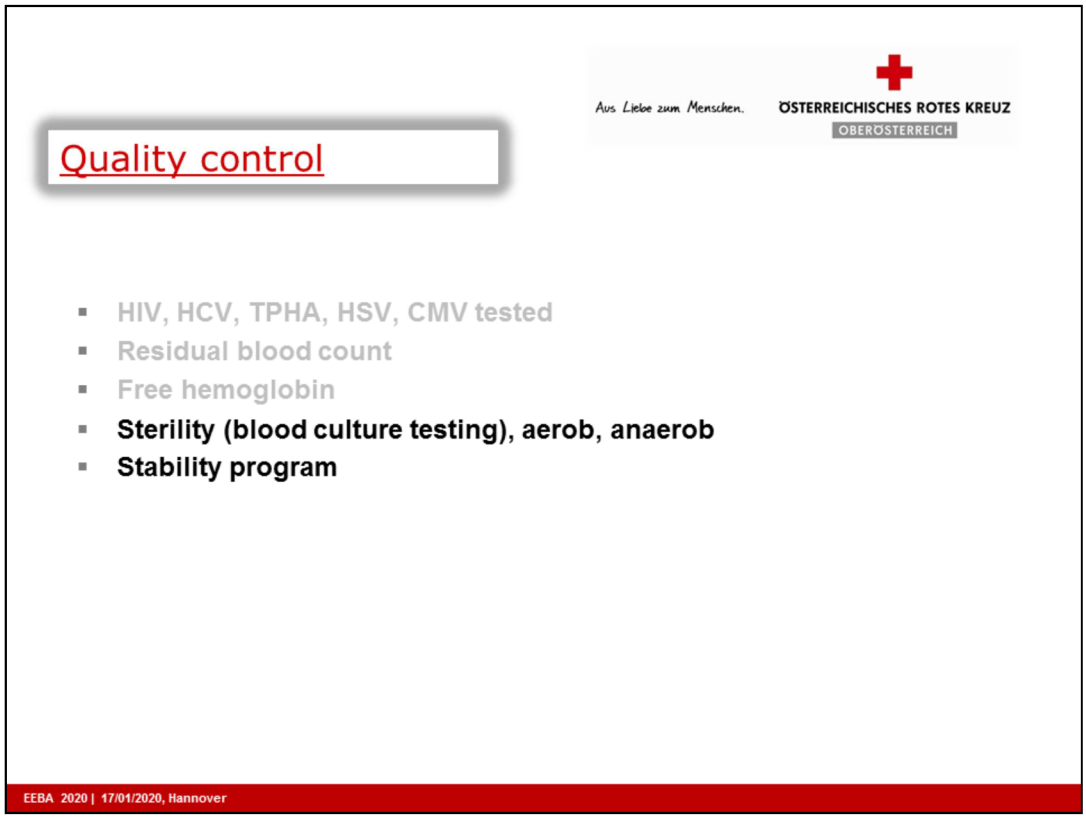

- QC performed contemporaneously for each product (infect marker, residual blood count, free hemoglobin and sterility)
- Additionally a yearly stability program is mandatory.

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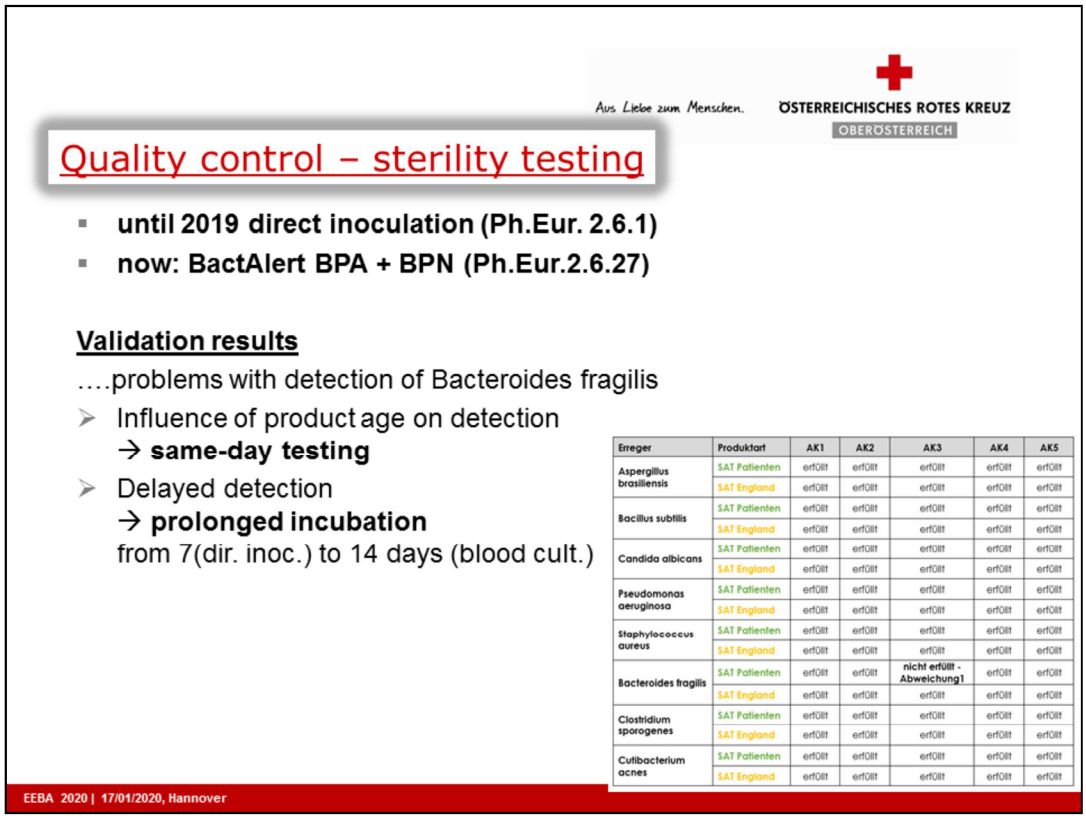

Erreger	Produktart	AK1	AK2	AK3	AK4	AK5
Aspergillus brasiliensis	SAT Patienten	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
	SAT England	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
Bacillus subtilis	SAT Patienten	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
	SAT England	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
Candida albicans	SAT Patienten	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
	SAT England	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
Pseudomonas aeruginosa	SAT Patienten	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
	SAT England	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
Staphylococcus aureus	SAT Patienten	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
	SAT England	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
Bacteroides fragilis	SAT Patienten	erfüllt	erfüllt	nicht erfüllt - Abweichung1	erfüllt	erfüllt
	SAT England	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
Clostridium sporogenes	SAT Patienten	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
	SAT England	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
Cutibacterium acnes	SAT Patienten	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt
	SAT England	erfüllt	erfüllt	erfüllt	erfüllt	erfüllt

- Up to end of 2019 obliged to perform direct inoculation for SED sterility testing (according to Ph.Eur. 2.6.1) within a LAF class A with background B
- Requirements changed → back with sterility testing with blood culture testing (BactAlert System) with inoculation in a LAF class A with background D
- During method validation one deviation found → problems with detection of bacterioides fragilis

a) product age has impact (testing needs to be started on day of production)

b) delay in detection (incubation time to be prolonged)

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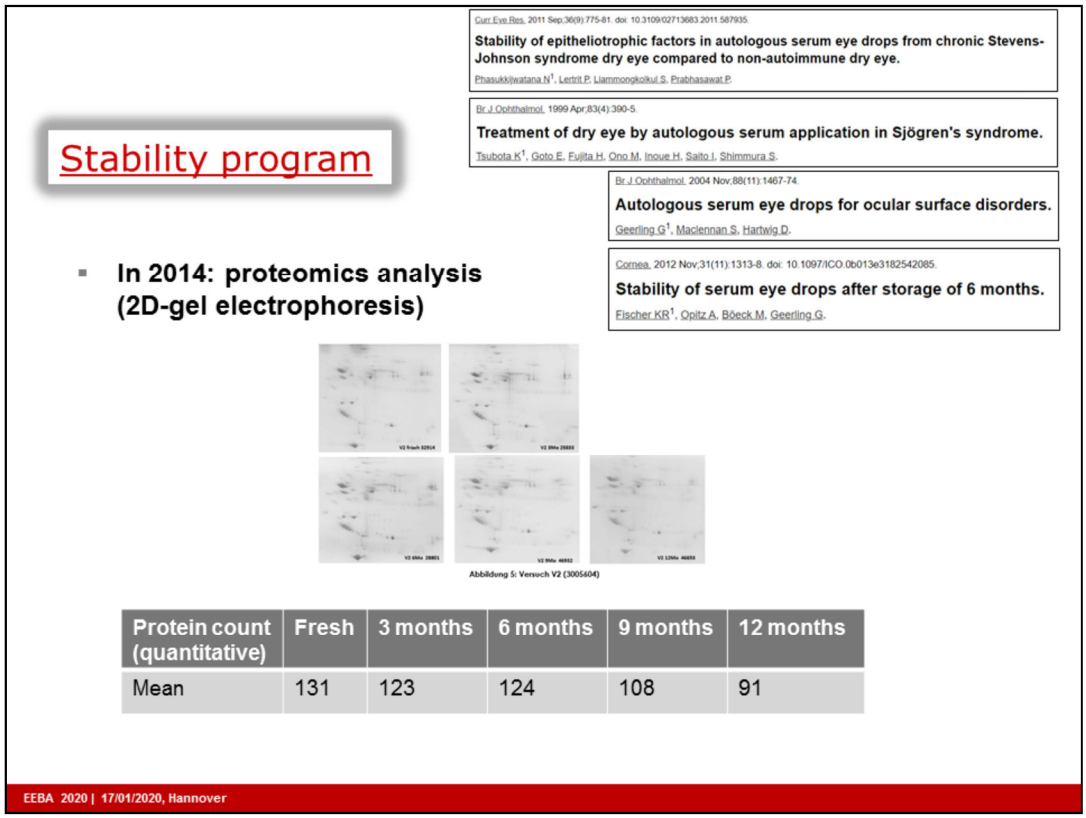

Stability testing as additional requirement for medicinal products

First step was to assess shelf life:

- several surrogate proteins chosen on the basis of literature research → EGF (endothelial growth factor), PDGF (platelet derived growth factor), fibronectin → proteomic analysis with 2D-gel electrophoresis → stable protein count for up to 6 months accompanied by negative sterility testing

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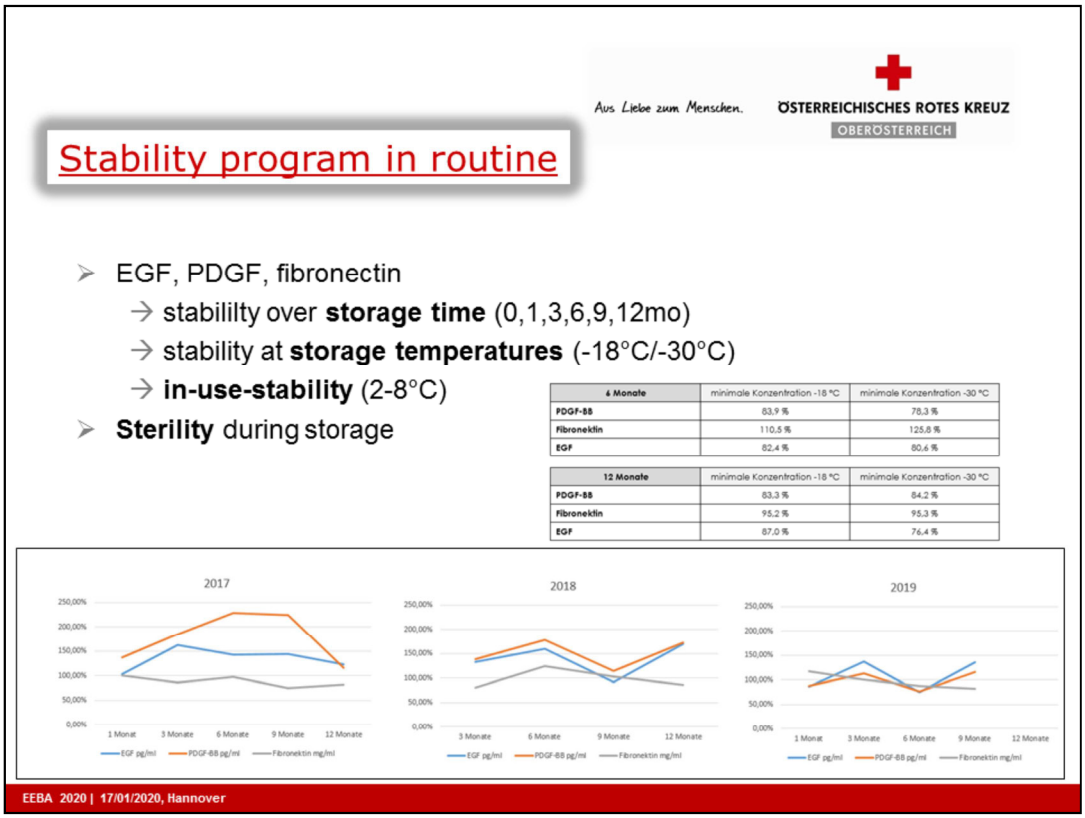

Since 2017 our SED stability program is performed routinely. Surrogate proteins are tested for storage time and temperature in order to constantly monitor quality of SED.

- Surrogate proteins stable for up to 6 months/ no difference between -30°C storage at blood bank and -18°C in domestic freezer/ all SED remained sterile
- In-use stability testing to be established to verify that quality can be retained in one receptacle for one day, once container is opened by patient
- In-use stability testing performed after 3 months → after first use of container a drop was squeezed out every two hours (in-between storage at 2-8°C) → surrogate proteins and sterility tested and comparable to stability data at same time point

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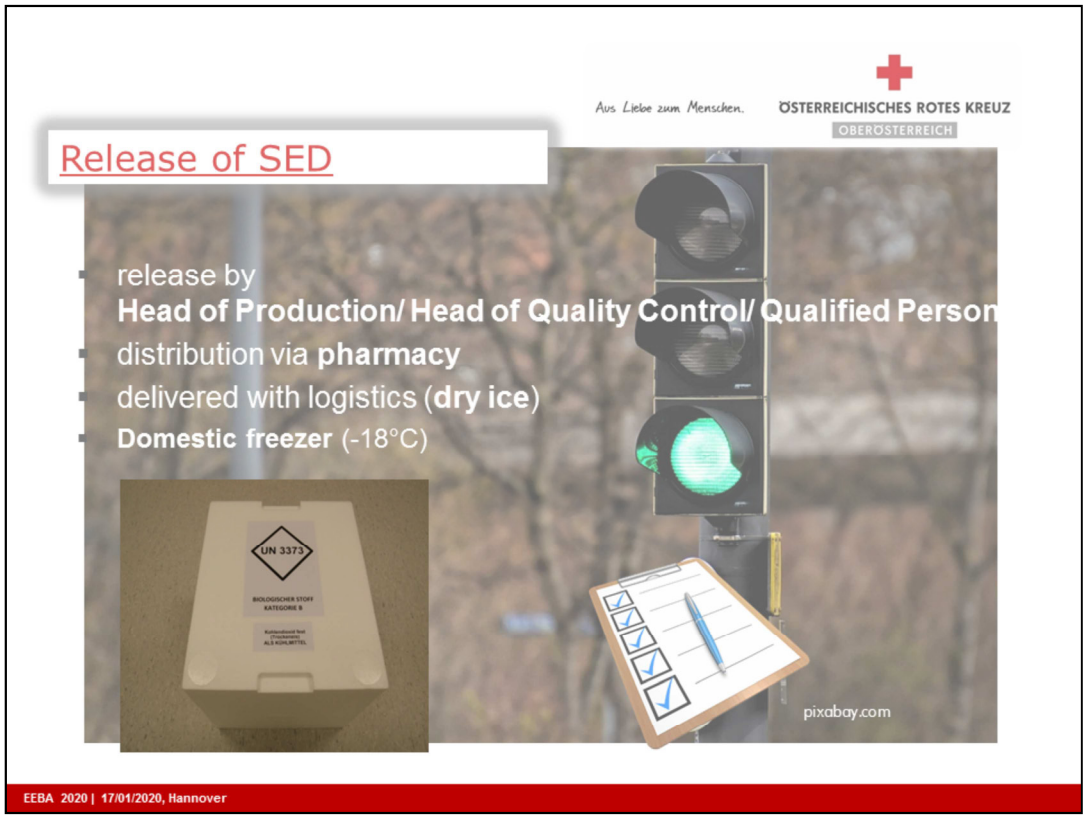

Some additional requirements need to be fulfilled also when distributing SED

- SED need to be officially released by Head of Production, Head of Quality Control and Qualified Person
- Only then SED can be distributed, but formally only by a pharmacy.

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