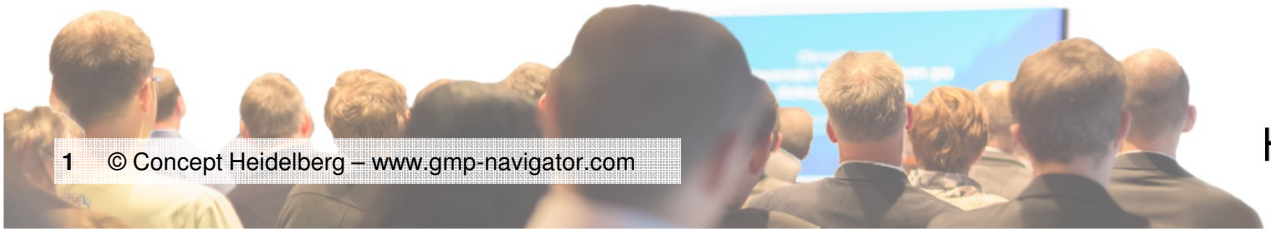
Strahlenschutz in der Produktion von Radiopharmazeutika

Gerald Reischl

Mannheim
29.09.2015



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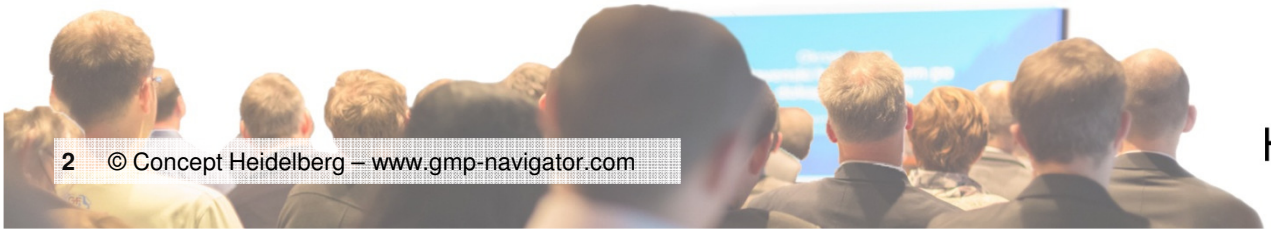
Gliederung

- Gesamtkonzept einer Anlage
- Strahlenschutzschleuse (Personal)
- Produktion Isotope (Beispiel PET / Zyklotron)
- Verteilung Isotope
- Synthese Radiopharmaka (Abzüge, Heißzellen)
- Abfüllung Radiopharmaka (Isolator)
- Verpackung / Transport
- Monitoring (Räume, Personen)
- Abfälle / Entsorgung



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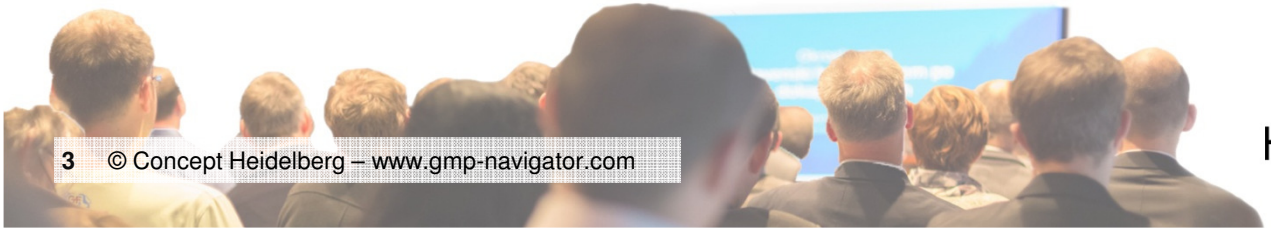

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Regulatorische Anforderungen I

Strahlenschutz (StrSchV):

- Strahlenschutzbereiche
- Zugangskontrolle, Monitoring
- Lüftung (negativer Druck)

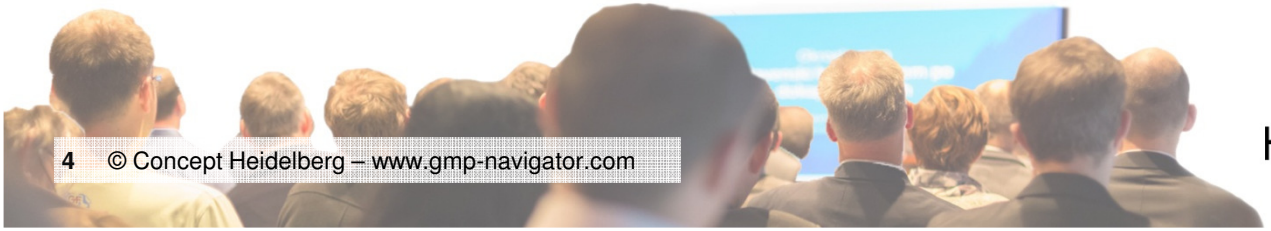
↑

Produktion von Radiopharmazeutika

↓

Arzneimittel-Sicherheit (AMG, GMP):

- Reinräume (Herstellung: C, Abfüllung: A)
- Umgebungs-Monitoring (Druck, T, Feuchte)
- Lüftung (positiver Druck)



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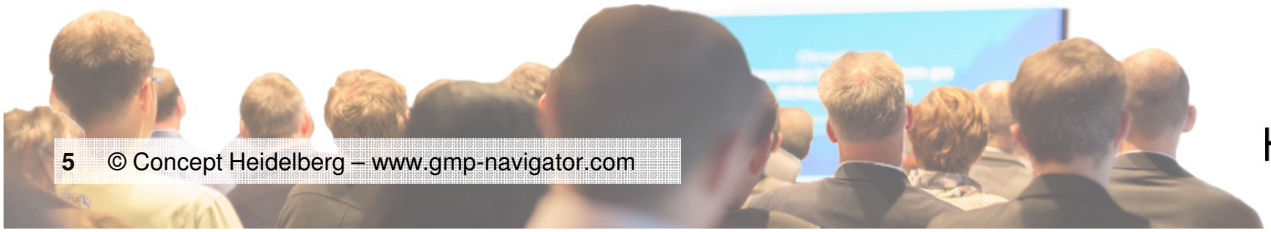
Regulatorische Anforderungen II

Strahlenschutz PET-Radiopharmazie:

- **Betriebsgenehmigung Zyklotron**
- **Labore SSK 3 (ohne Zyklotron SSK 2)**
- **Kontrollbereich (> 6 mSv/a)**
  (Zyklotron-Bunker Sperrbereich in Betrieb)
- **Mind. 10-facher Luftwechsel**
- **Unterdruck gegenüber Umgebung**
- **Umgangsgenehmigung UGG (Bsp. Tü):**

C-11	**700 GBq**
F-18	**300 GBq**
O-15	**300 GBq**
weitere	



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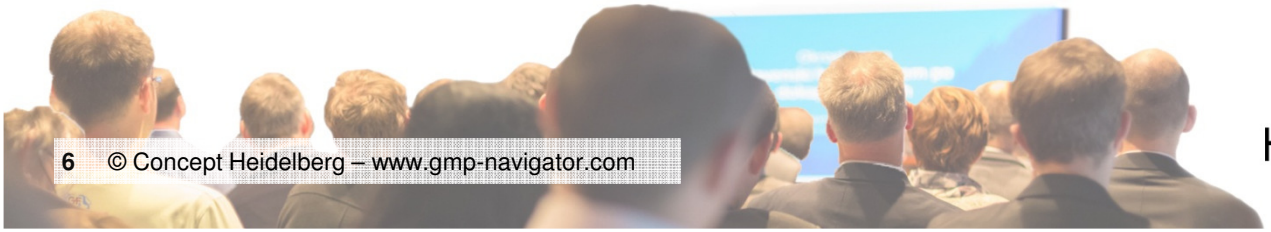
Anlagenkonzept

- Beispiel UNI Tübingen -



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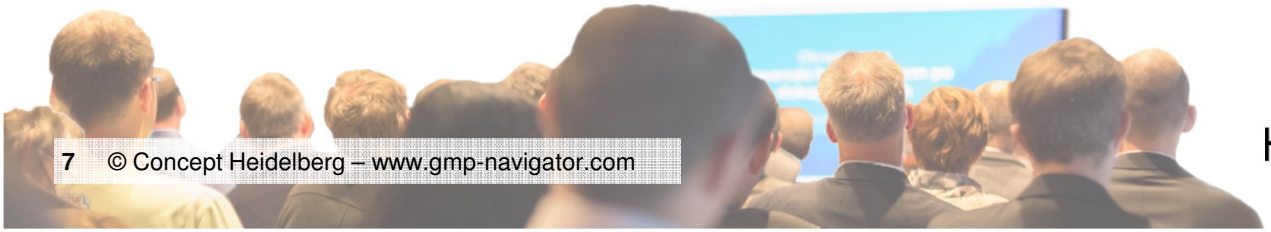

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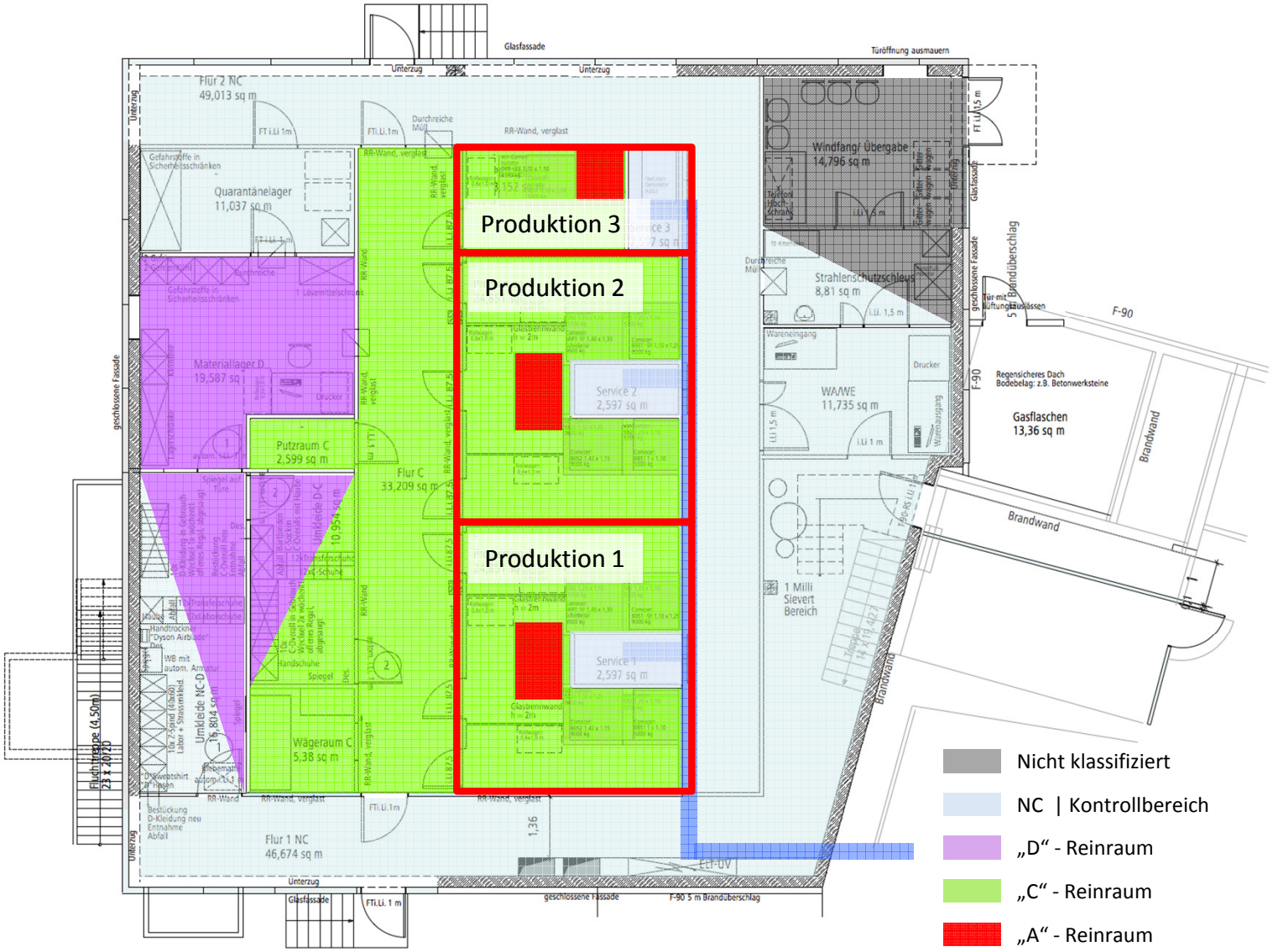

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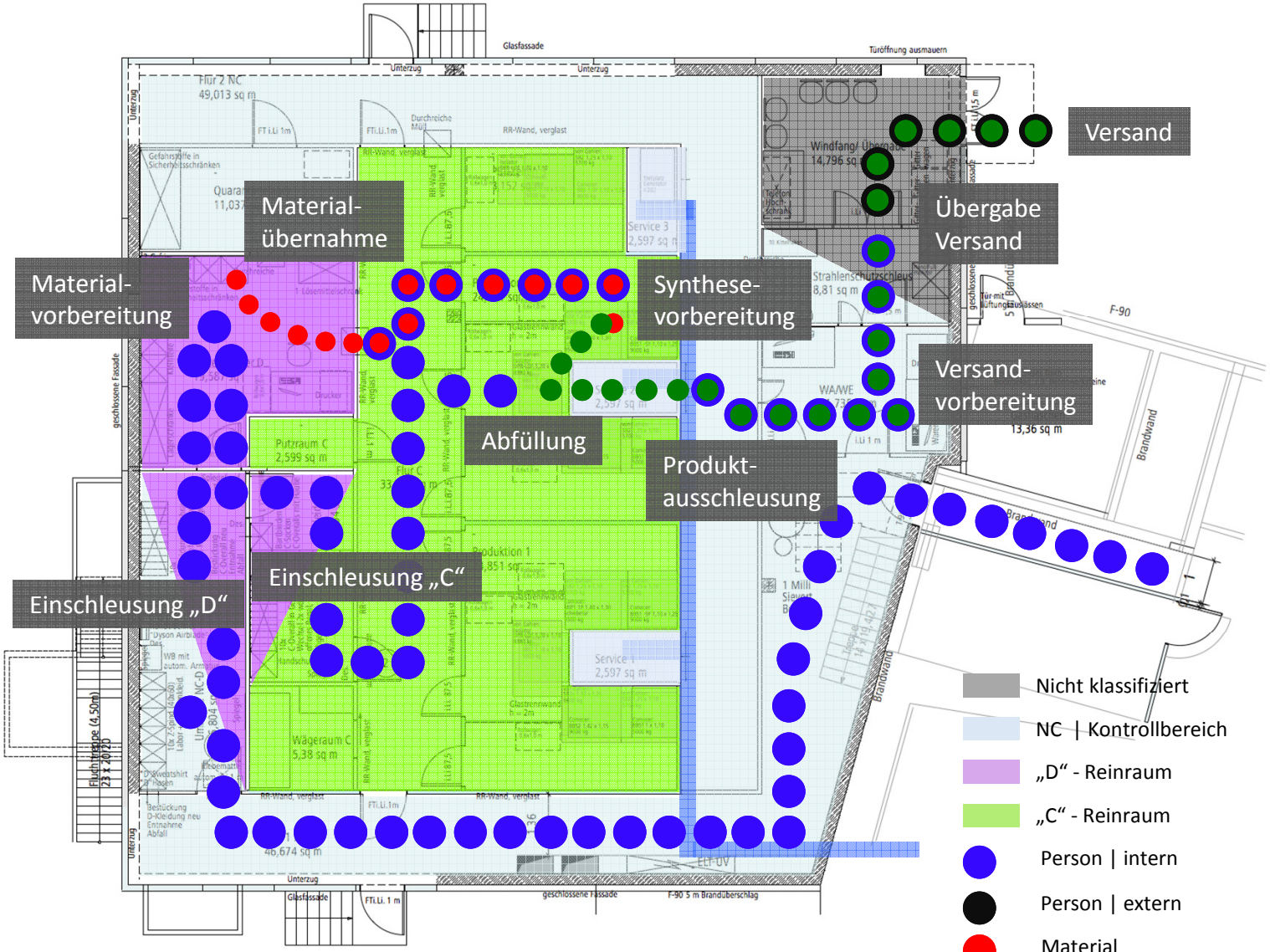

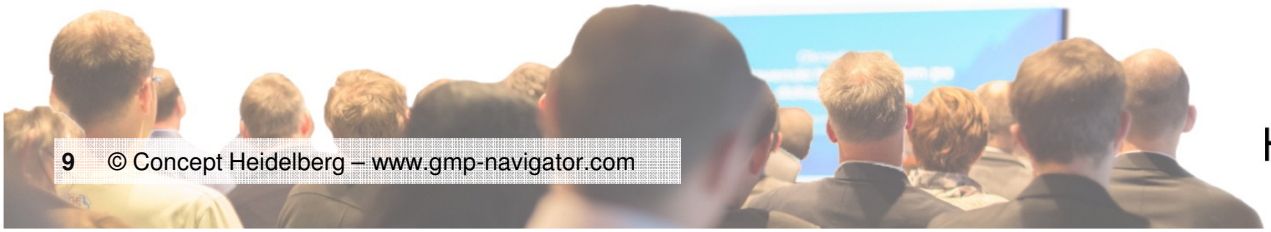

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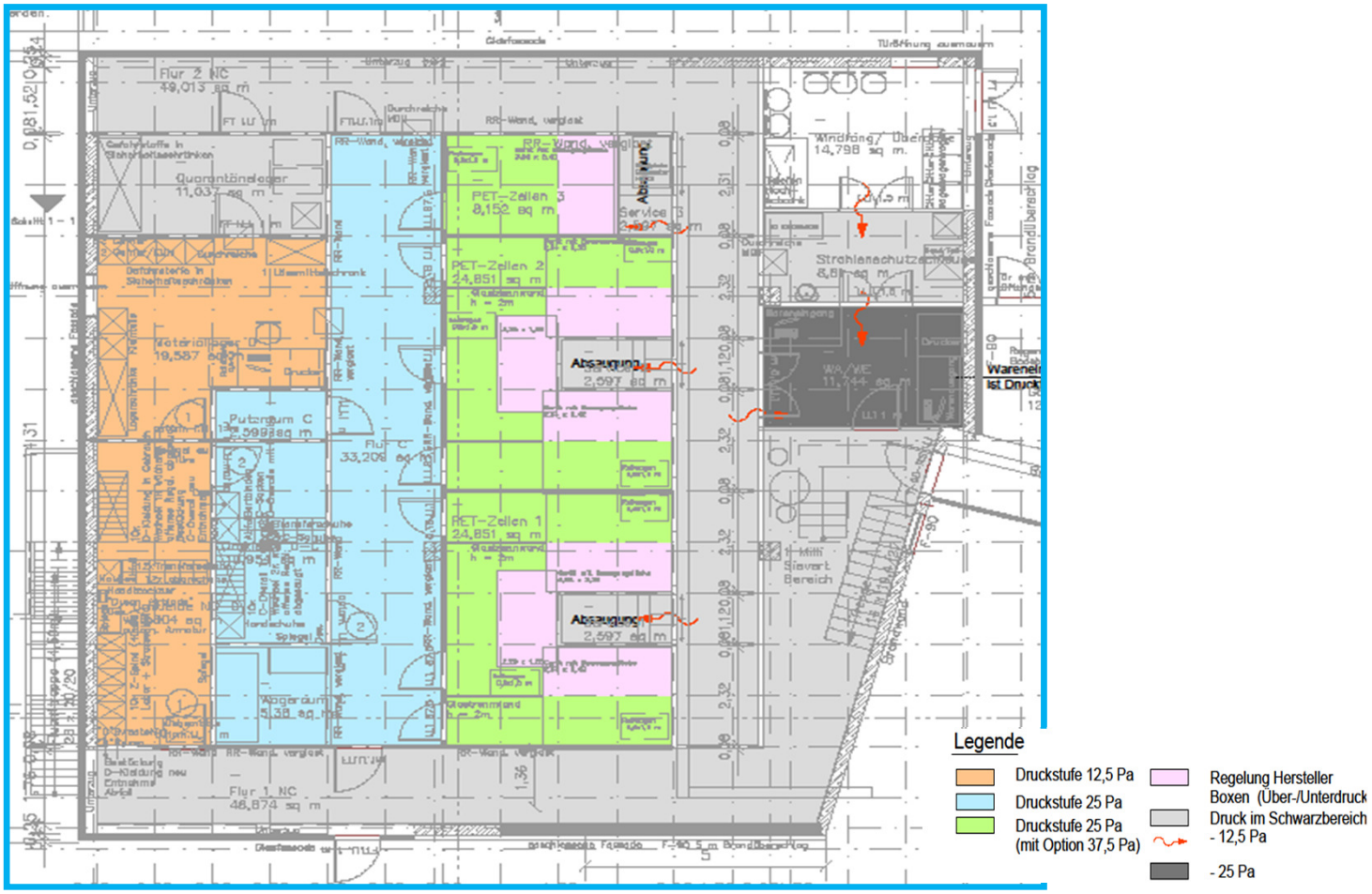
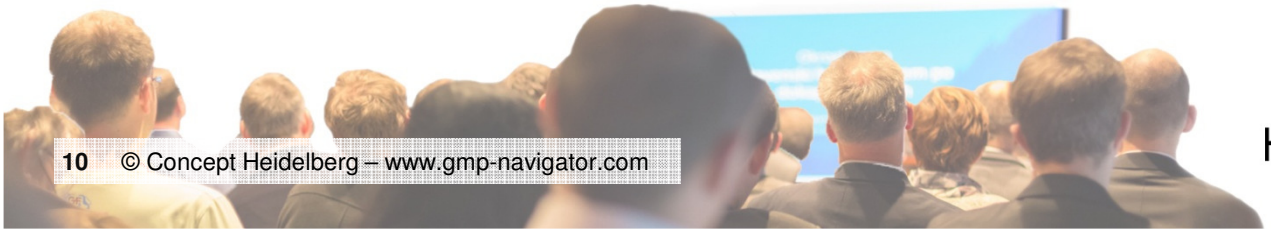
Druckstufen-Konzept





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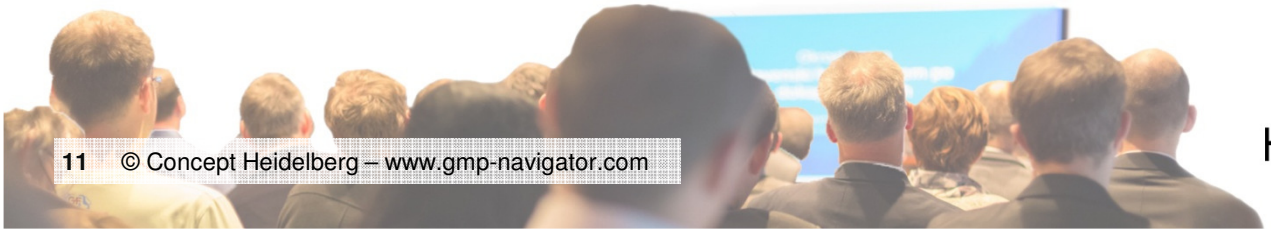

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Strahlenschutzschleuse I

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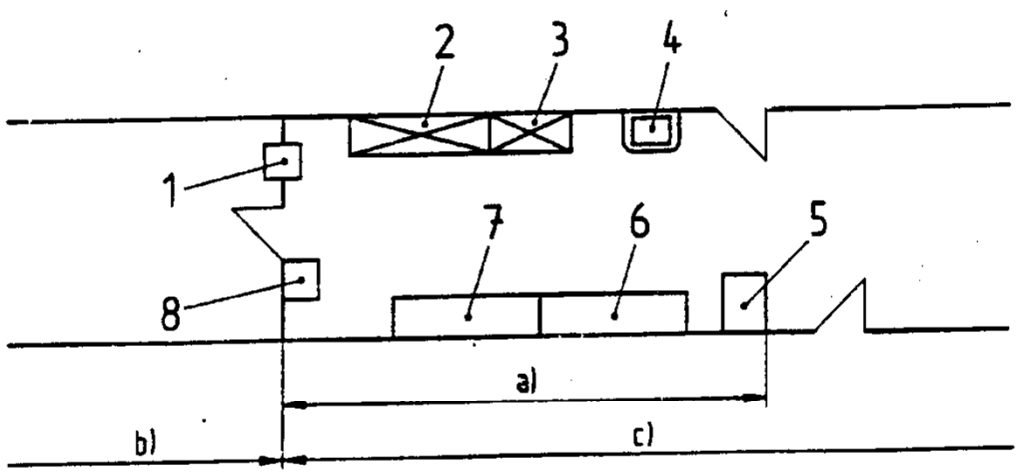
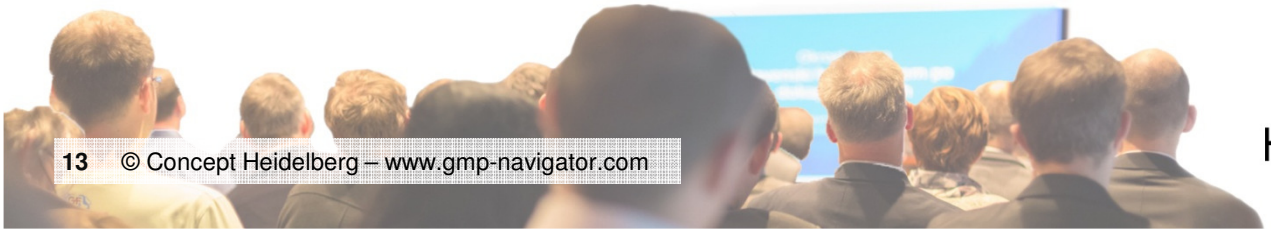
Strahlenschutzschleuse II



1 Vorrichtung zur Überwachung des Personenverkehrs
2 Vorratsschrank für Schutzkleidung
3 Behälter für kontaminierte Schutzkleidung
4 Handwaschbecken mit Handbrause
5 Hand-Fuß-Kleidermonitor
6 Hakenbrett für Schutzkleidung
7 Hakenbrett für konventionelle Labormäntel
8 Telefon

a) Schleuse b) konventioneller Bereich c) Radionuklidlaboratorium



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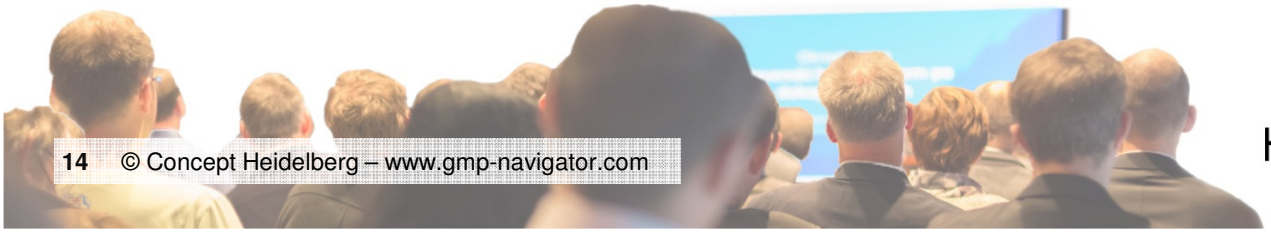

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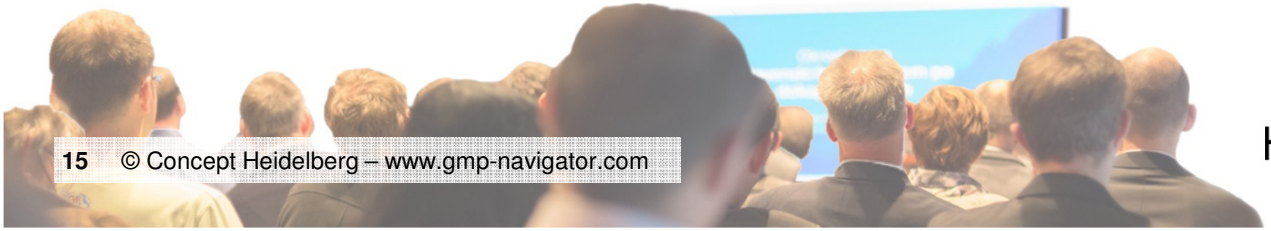
Zugang zum Zyklotron

- Anzeige Strahlbetrieb (dann Sperrbereich)
- Überwachung Gamma- und Neutronendosis (Vorraum) mit optischem und akustischem Alarm
- Sicherheits-Interlock Türen
- TÜV jährlich



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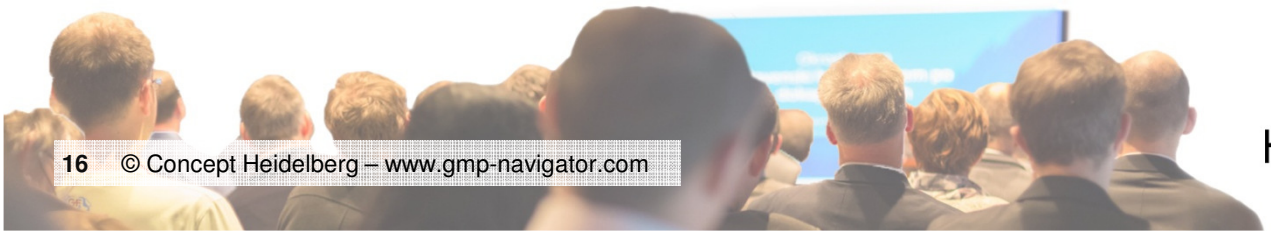
Besonderheiten der PET-Radionuklide

- **Neutronenarme Nuklide**
- **Emission von Positronen:**

  Proton → Neutron + Positron + Neutrino

- **Kurze Halbwertszeiten**



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Wichtige PET-Radionuklide

Nuklid	HWZ	Intensität ß⁺ / %	Kernreaktion	Bemerkungen
F-18	109.8 min	96.9	$^{18}O(p,n)^{18}F$	
C-11	20.4 min	99.8	$^{14}N(p,\alpha)^{11}C$	
N-13	9.98 min	100	$^{16}O(p, \alpha)^{13}N$	
O-15	2.03 min	99.9	$^{14}N(d,n)^{15}O$	Alternative: $^{15}N(p,n)^{15}O$
I-124	4.18 d	25	$^{124}Te(p,n)^{124}I$	
Y-86	14.7 h	33	$^{86}Sr(p,n)^{86}Y$	
Cu-64	12.7 h	17.9	$^{64}Ni(p,n)^{64}Cu$	Auch Therapie
Ga-68	68 min	90		Generatornuklid (Mutter Ge-68)

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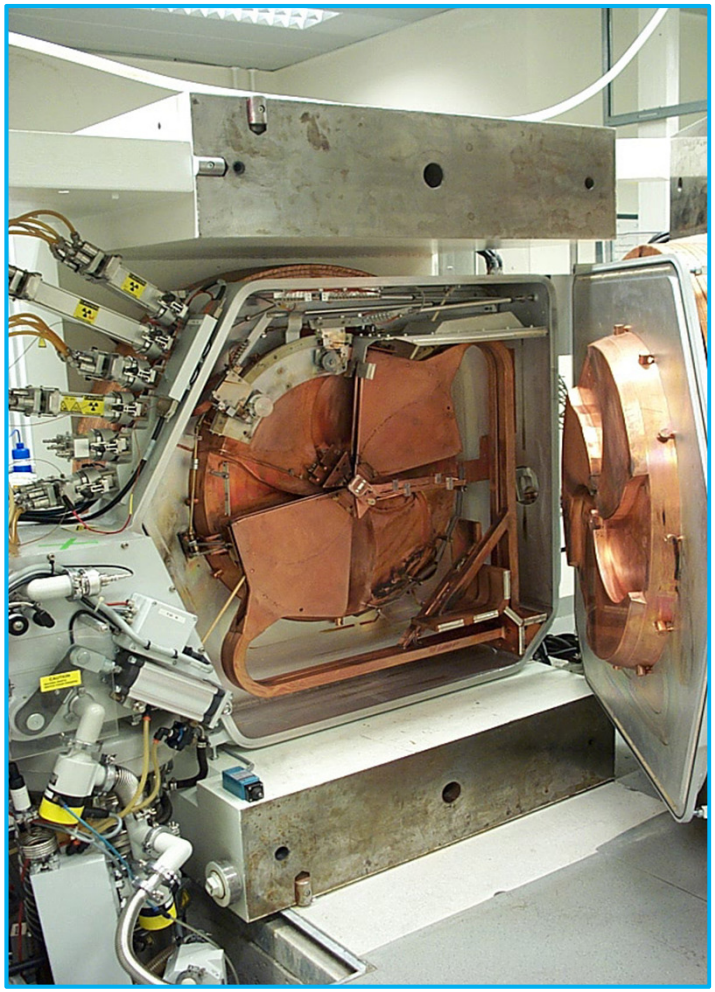
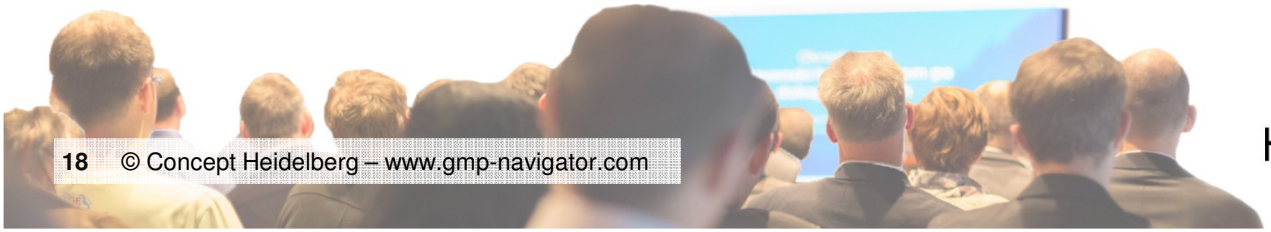
Zyklotron





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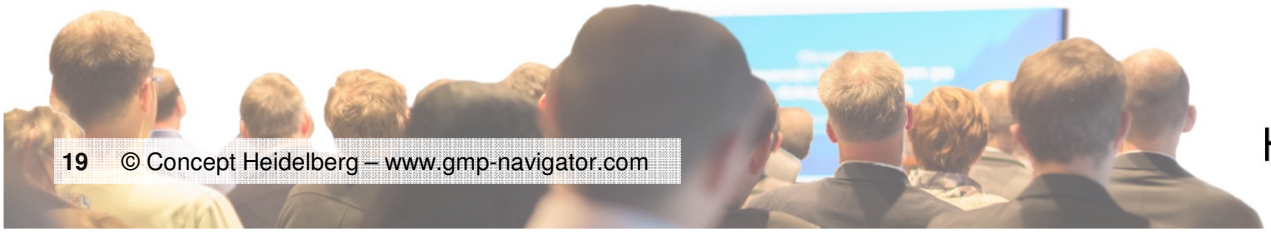
Kernreaktionen

$[^{18}O]H_2O$	$^{18}O(p,n)^{18}F$	$[^{18}F]Fluorid_{aq.}$
$N_2(1\ \%\ O_2)$	$^{14}N(p,\alpha)^{11}C$	$[^{11}C]CO_2/N_2$
H_2O	$^{16}O(p,\alpha)^{13}N$	$[^{13}N]Nitrat_{aq.}$
$N_2(1\ \%\ O_2)$	$^{14}N(d,n)^{15}O$	$[^{15}O]O_2/N_2$
$^{64}Ni_{metall.}$	$^{64}Ni(p,n)^{64}Cu$	$[^{64}Cu]Cu/Ni$

Feste, flüssige und gasförmige Bestrahlungsprodukte



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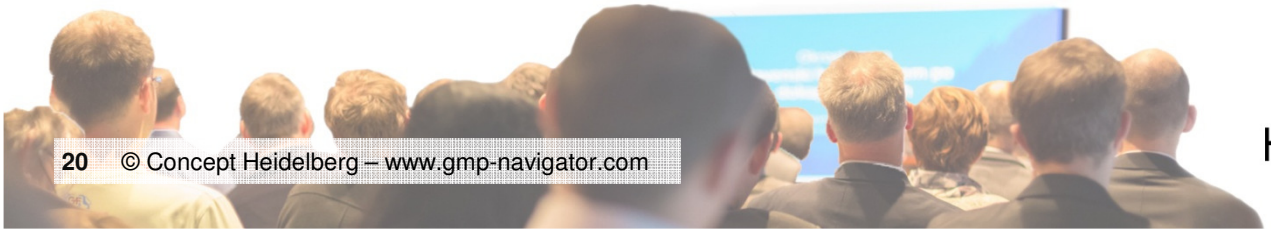

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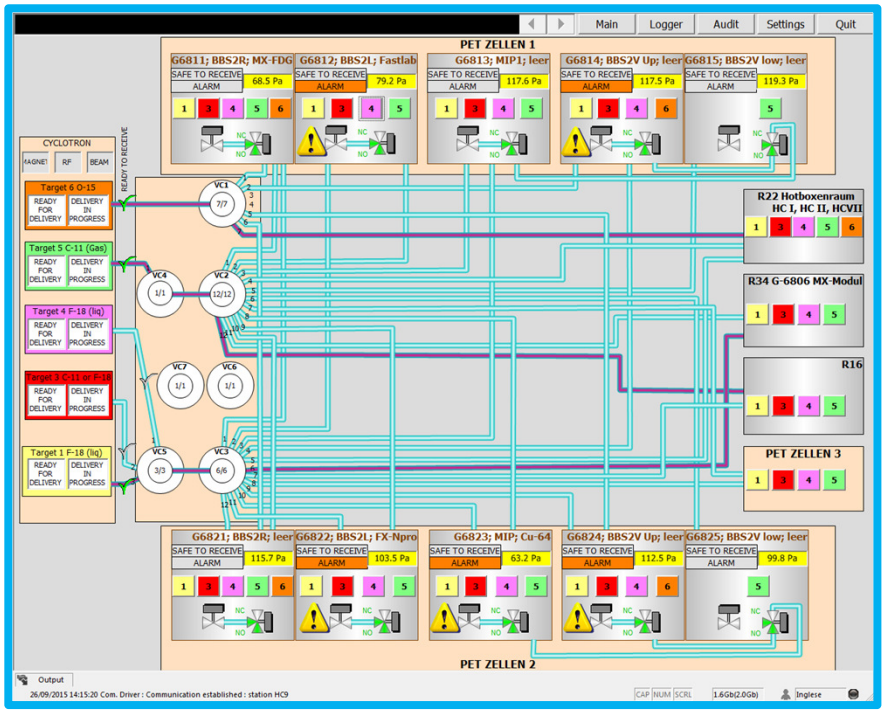
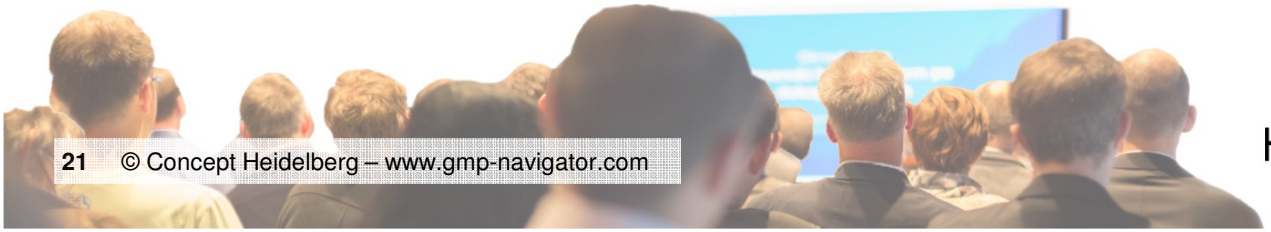
Isotop-Verteilung vom Zyklotron





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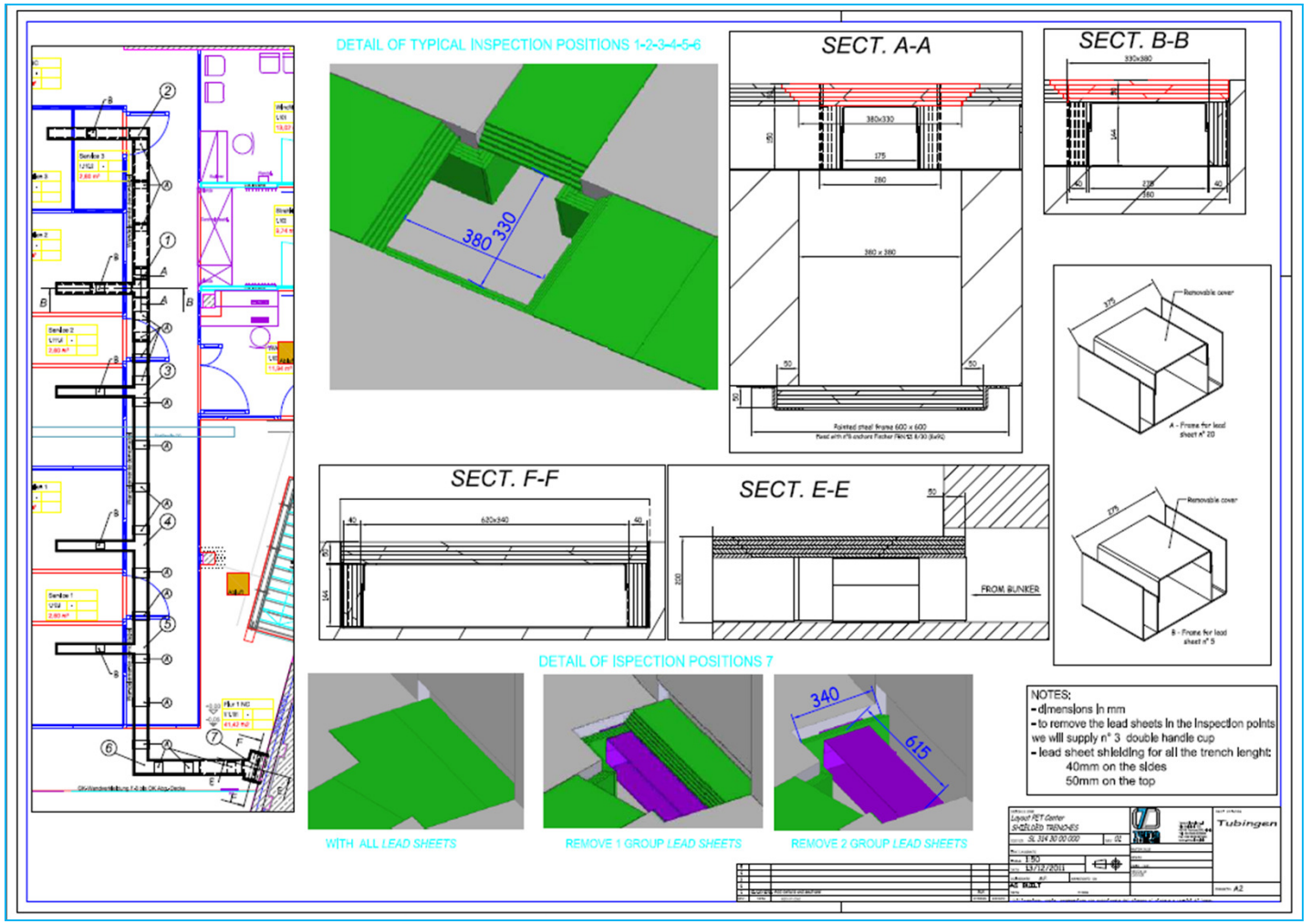
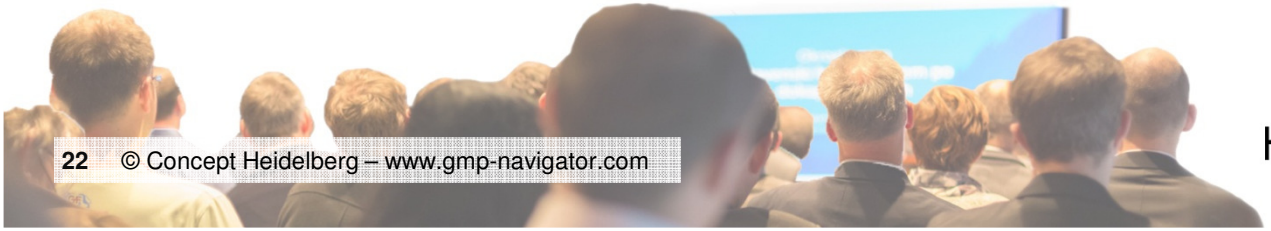
Isotop-Verteilung

- Bodenkanal -





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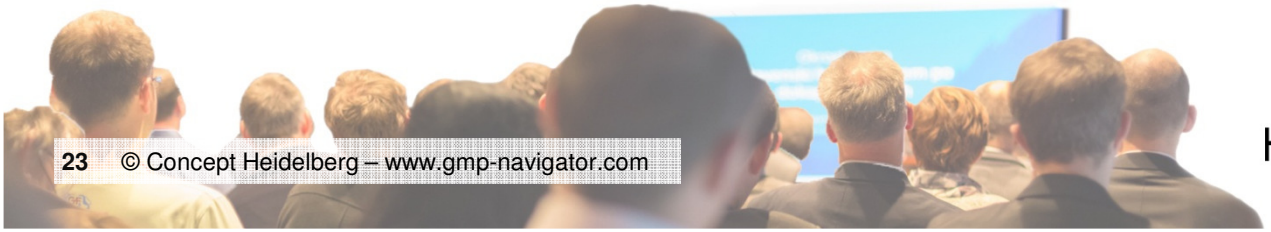

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Radionuklidabzug

Mit Filterkasten

Arbeitsfläche
fugenlos als Wanne

Bleiburg mit
Bleiglasfenster
(Tragkraft !)

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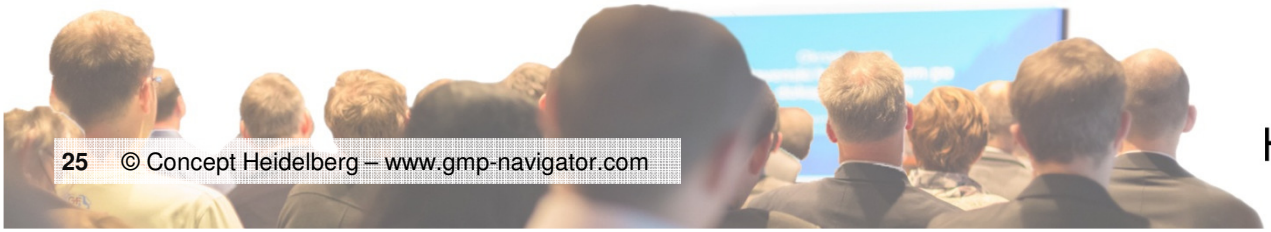
Radionuklidabzug

- Unterbau und Versorgung -

Abfälle

- Wasserzuleitung nur für Kühlwasser Ableitung überhöht über Arbeitsfläche (normales Abwasser)
- Steckdosen und Stecker im Innern gegen Kontamination schützen
- Bedienelemente außen



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Personal- und Materialschleusen Reinraum

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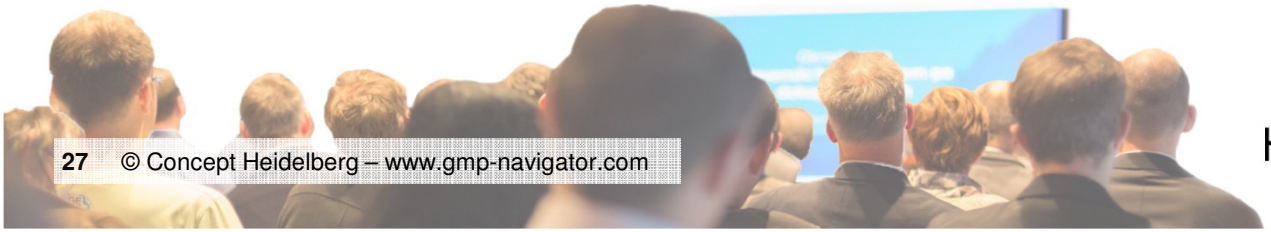
Herstellung Reinraum C

- Heißzellen und Synthesemodule -



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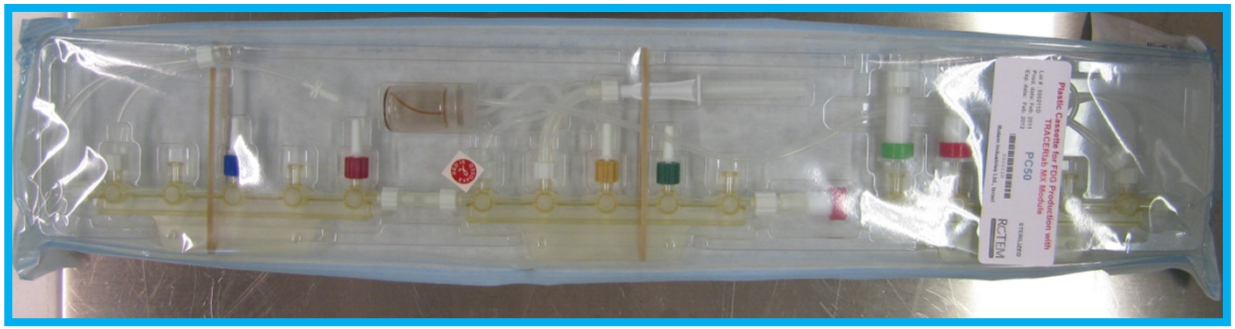
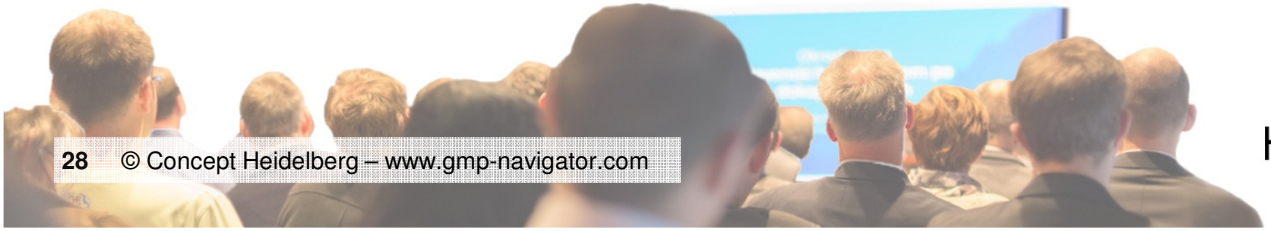
Herstellung Reinraum C

- Automatisierte Synthese -





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PET-Nuklide und Strahlenschutz

- Abstand -

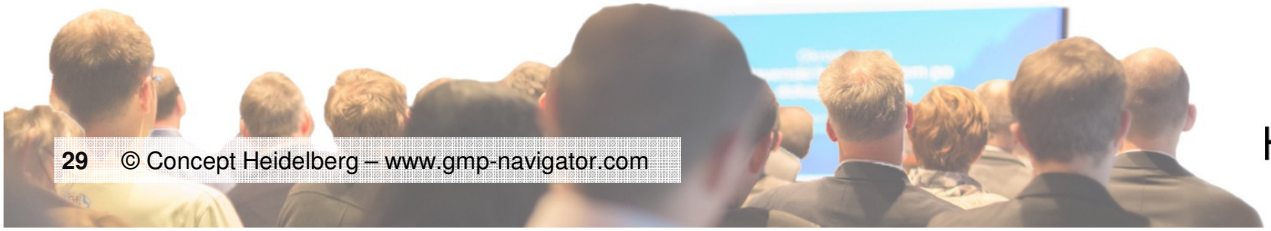
Vernichtungsstrahlung 511 keV

$$\text{Ortsdosisleistung}[\text{mSv}] = f \cdot t[\text{h}] \cdot A[\text{GBq}] \cdot d^{-2}\left[\text{m}^2\right]$$

$$f\,(F-18) = 1{,}59 \cdot 10^{-1}\,\text{mSv} \cdot \text{m}^2 \cdot \text{h}^{-1} \cdot \text{GBq}^{-1}$$

Beispiel: 100 GBq

Abstand:	Ortsdosisleistung:	
100 cm	0,0159 Sv/h	265 µSv/min
10 cm	1,59 Sv/h	26,5 mSv/min
1 cm	159,0 Sv/h	2,65 Sv/min



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PET-Nuklide und Strahlenschutz - Abschwächung in Blei -

Vernichtungsstrahlung 511 keV

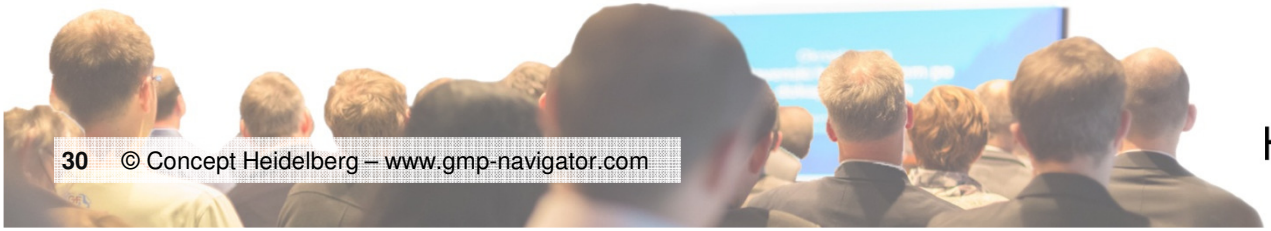
$$\frac{N(d)}{N(0)} = e^{-\mu \cdot \rho \cdot d}$$

μ = 0,13 $cm^2 \cdot g^{-1}$
ρ = 11,35 $g \cdot cm^{-3}$
d = Materialdicke/cm

d/cm	N(d)/N(O)
1	0,23
2	0,05
3	0,01
4	0,03
5	0,0006
10	$4 \cdot 10^{-7}$

Beispiel: 100 GBq

10 cm Abstand	1,59 Sv/h
5 cm Bleiabschirmung	0,95 mSv/h
10 cm Bleiabschirmung	0,64 µSv/h



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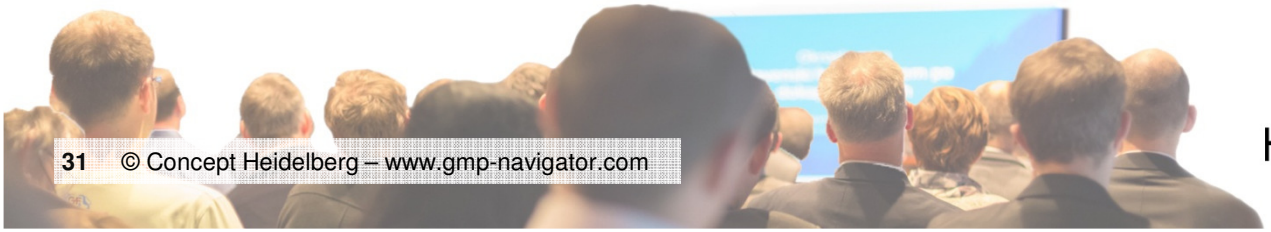
Gliederung

- Gesamtkonzept einer Anlage
- Strahlenschutzschleuse (Personal)
- Produktion Isotope (Beispiel PET / Zyklotron)
- Verteilung Isotope
- Synthese Radiopharmaka (Abzüge, Heißzellen)
- Abfüllung Radiopharmaka (Isolator)
- Verpackung / Transport
- Monitoring (Räume, Personen)
- Abfälle / Entsorgung



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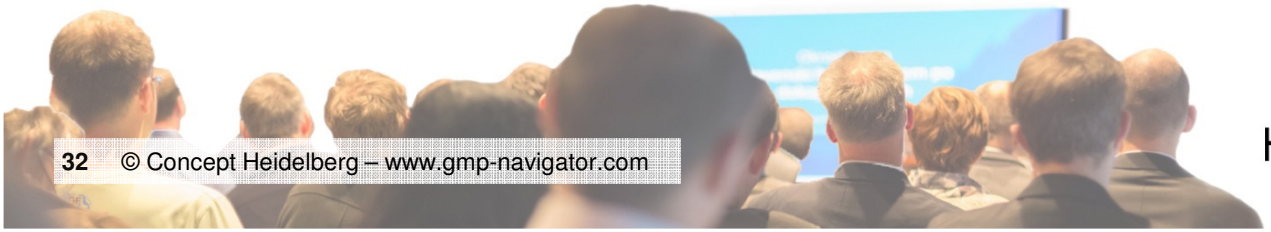
Isolator-Abfüllung

- Reinraum A -



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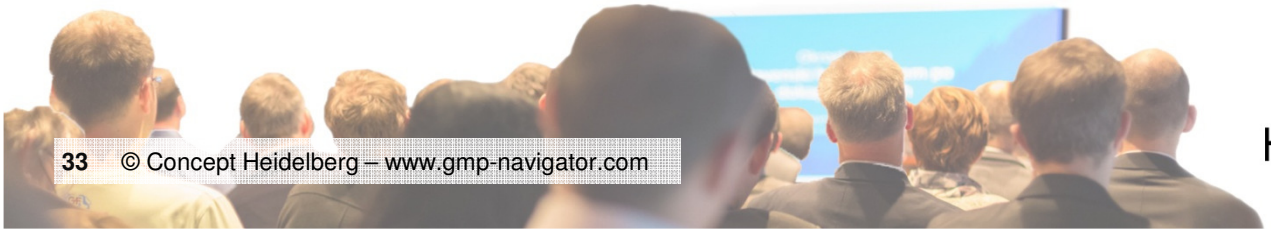

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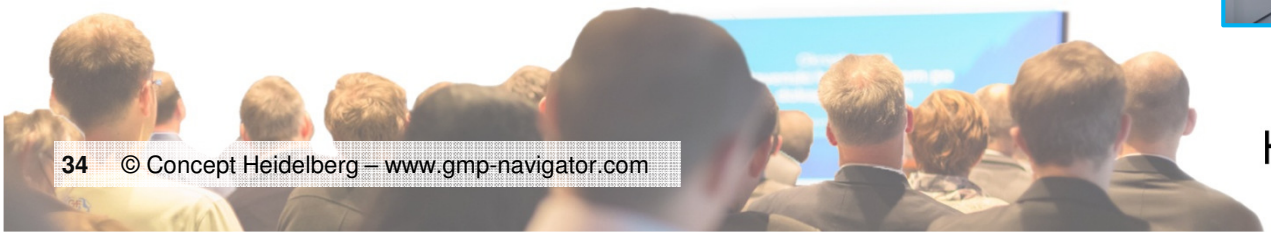
Ausschleusung, Verpackung, Transport

Rückseite Isolator, NC



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Versand (Behälter Type A)

Fluor-18 (FDG) **10.0 GBq**

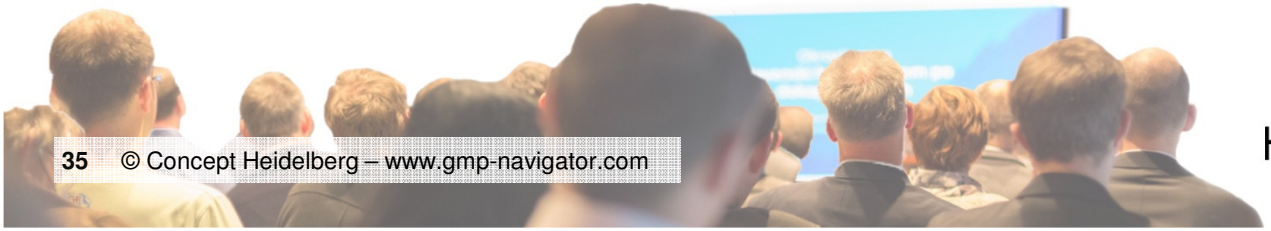
TK: 0.6, Oberfläche: 300 µSv/h (II, gelb)

Fluor-18 (Fluorid) **60.0 GBq**

TK: 6, Oberfläche: 3500 µSv/h (III, gelb)

Yttrium-86 **0.8 GBq**

TK: 10, Oberfläche: 7100 µSv/h (III gelb, u. a. V.)



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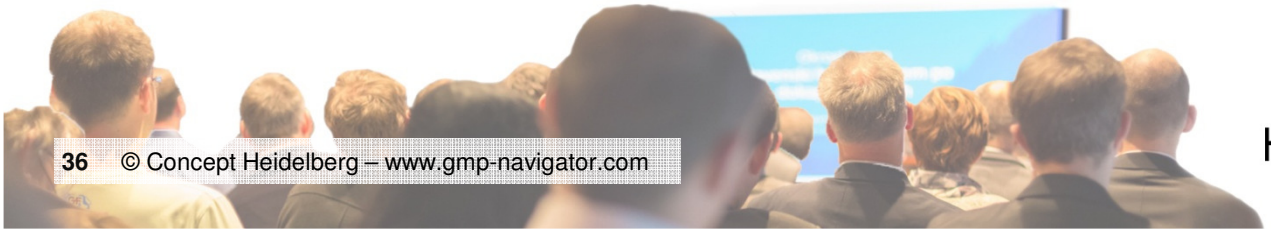

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Abwasseranlage

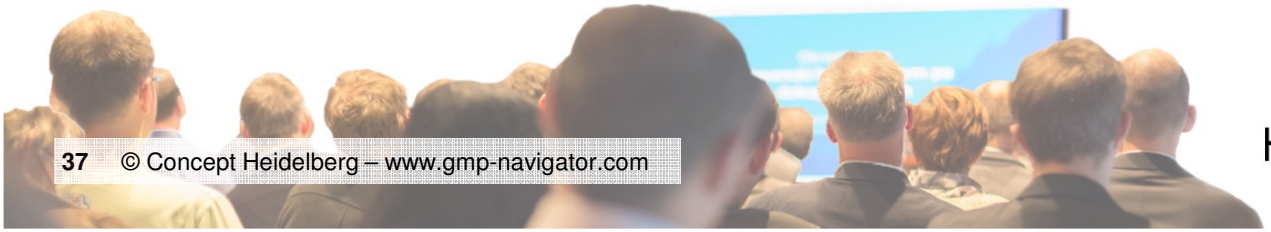
- Bsp. Isotopenlabor UNI Tübingen -

Schaltpult

Überwachung

Tanks

Pumpensumpf



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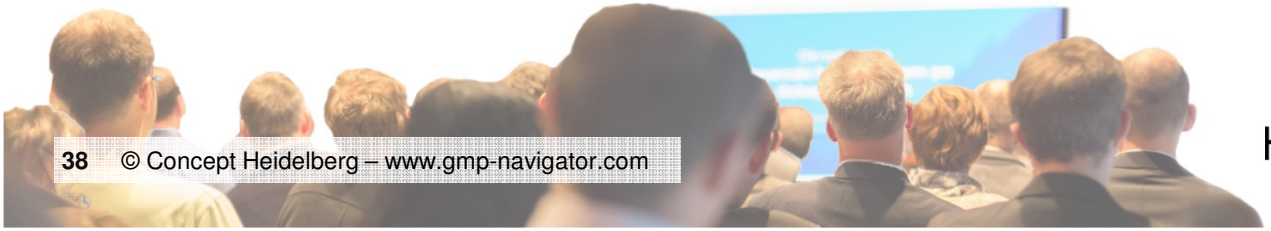
Abluft-Überwachung I

- Radiopharmazie UNI Tübingen -

- Überwachung der Raumdrucke (optischer und akustischer Alarm)
- Bilanzierende Messstelle Gesamtabluft (Grenzwert Jahresmittel)
- Messung Abluftkanäle gekoppelt mit Schnellschlußklappen zur Vermeidung von Freisetzungen (optischer und akustischer Alarm)
- Verpressung hochkontaminierter Abluft während Herstellung, zeitverzögerte Abgabe nach Abklingen



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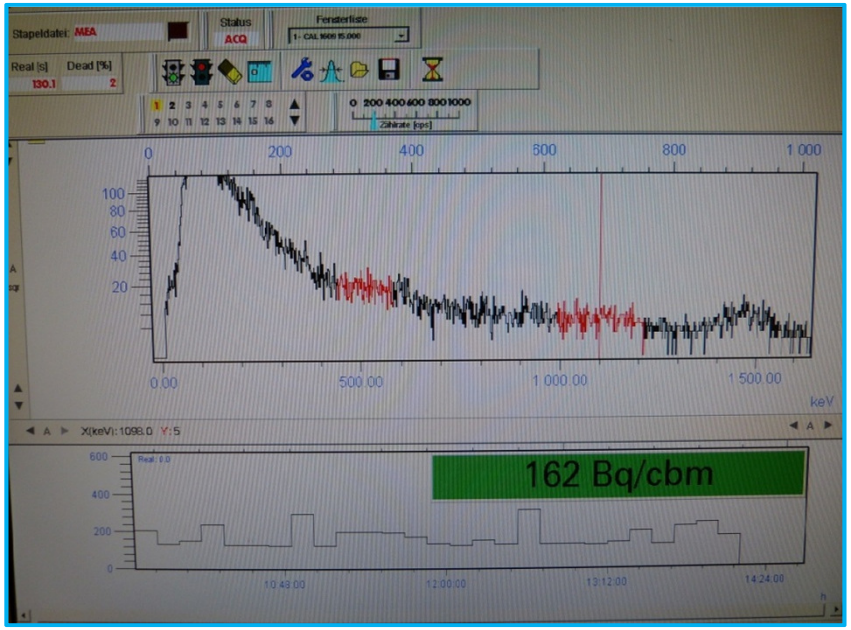
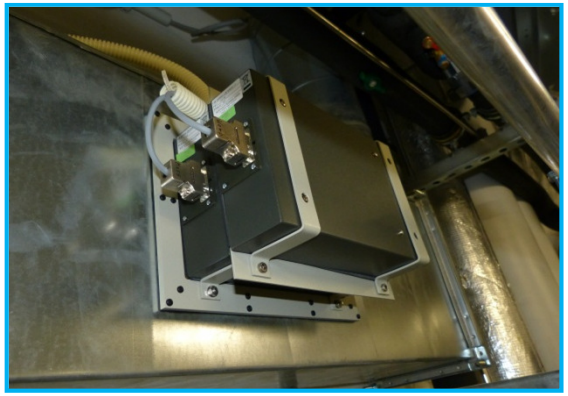
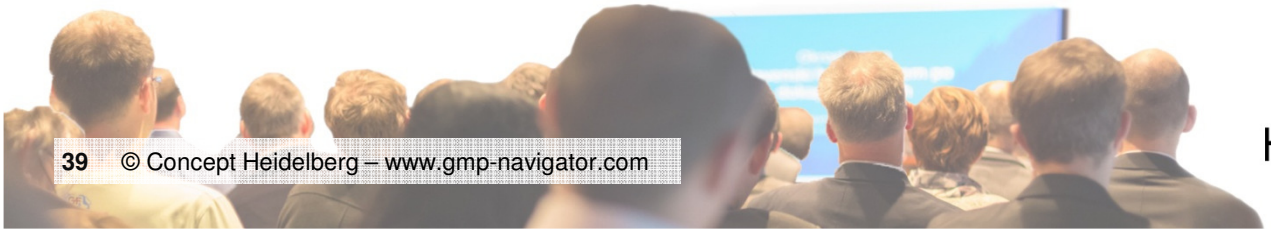
Abluft-Überwachung II

1. Bilanzierende Messstelle



2. Schnellschlussklappen





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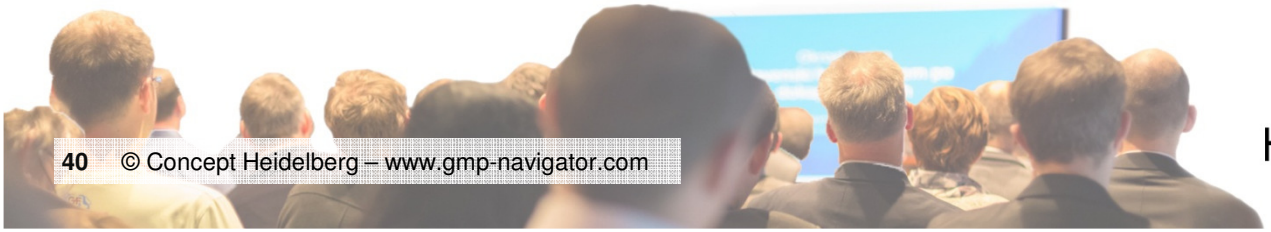
Verpressungsanlage

- **2 Kompressoren (Redundanz + Kapazität)**
- **4 x 4 Druckflaschen (je 50 l und 300 bar; wechselweise Befüllung)**



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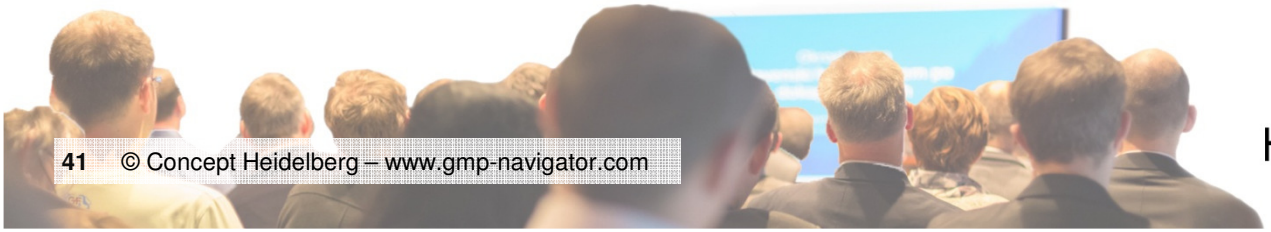
Dosisüberwachung Räume



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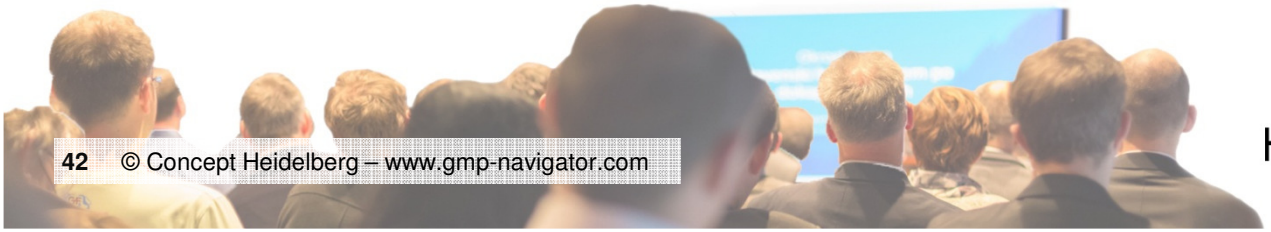
Dosisüberwachung Personal

- Filmdosimeter (amtl.)
- Ringdosimeter (amtl.)
- Ringdosimeter (wöchentl., zeitnahe Kontrolle, optional)
- Elektronisches Dosimeter (geeicht, mit Alarmschwelle)
- Überwachung Neutronendosis (Albedo) nicht zwingend am Zyklotron



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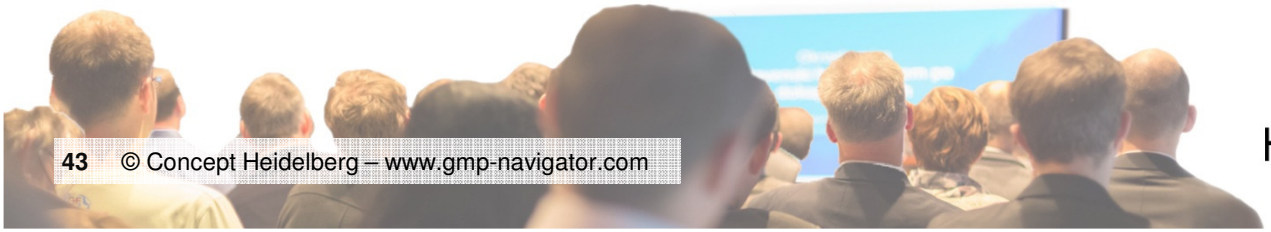

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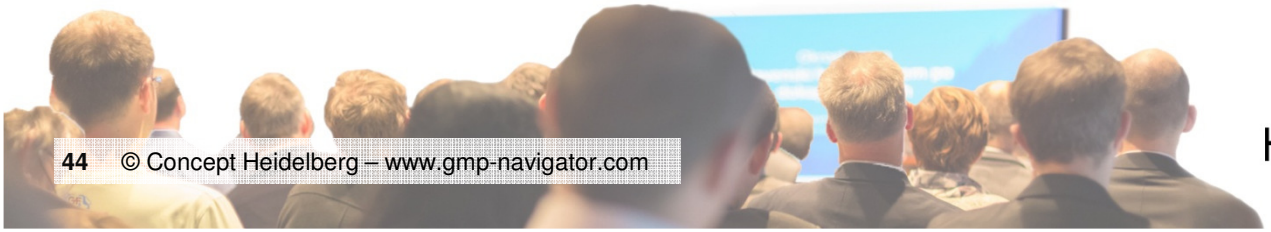
Abfälle

- langlebige Aktivierung im Zykotronbereich -



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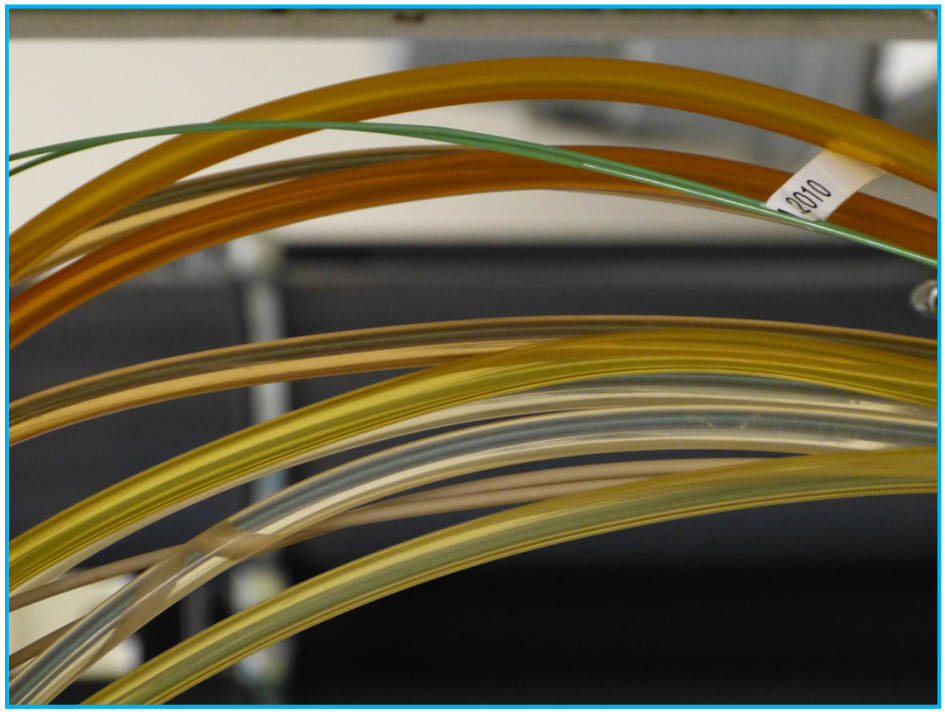
Haltbarkeit Materialien

- Alterung durch Radiolyse -



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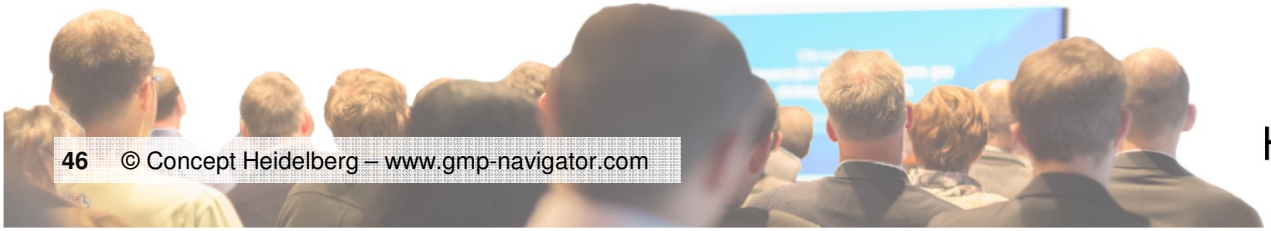
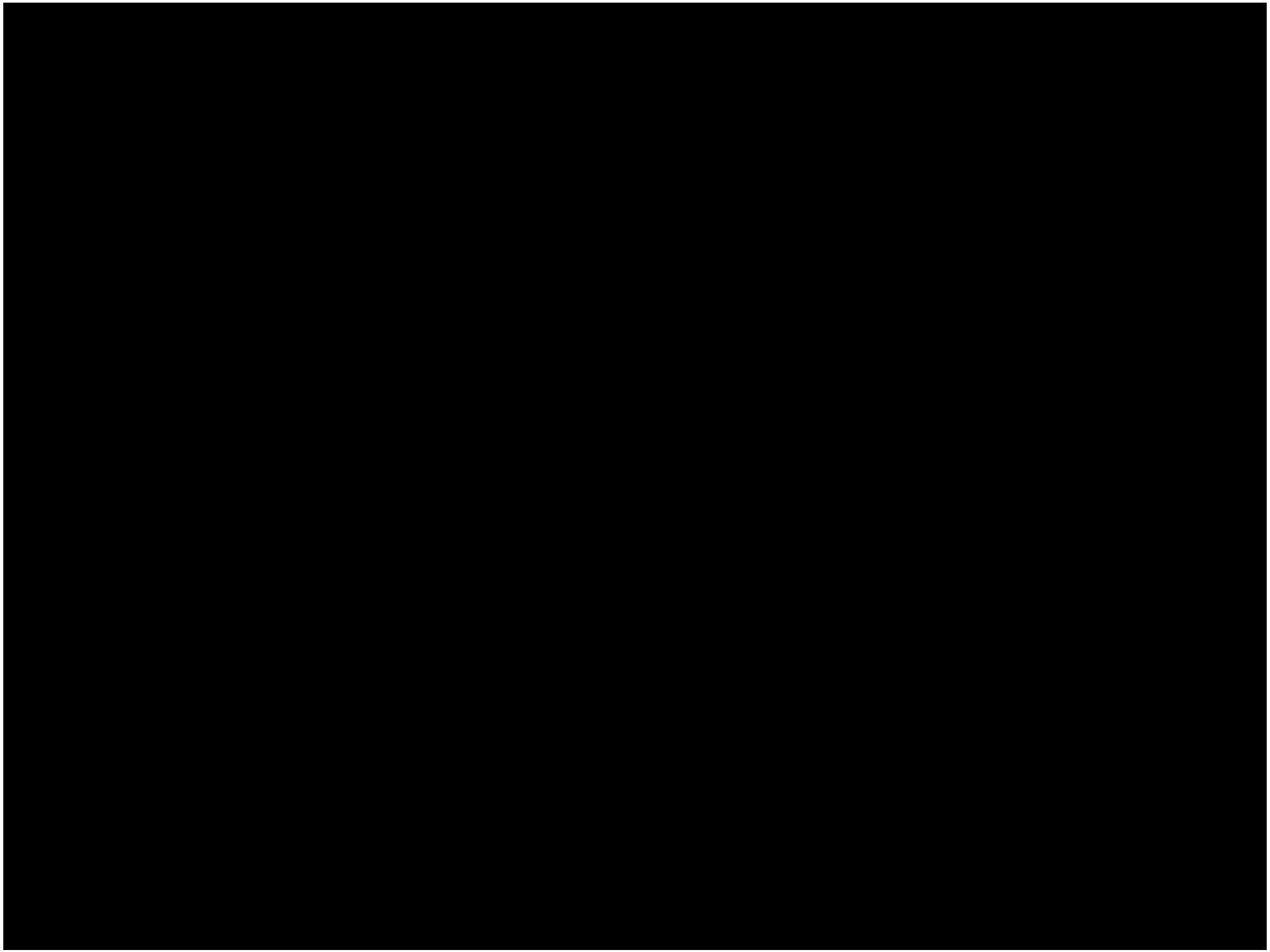
Abschließende Bewertung

- Herstellung Radiopharmazeutika streng reguliert (Strahlenschutz und Arzneimittelrecht)
- Überwachung Strahlenschutz und Arzneimittelherstellung Länderhoheit (regionale Unterschiede)
- Aufwändige Infrastruktur (kostenintensiv ↔ begrenzter Markt)
- Ambivalenz: Kurze Halbwertszeiten: Entsorgung (++)
  Hohe Aktivitäten: Strahlenschutz Personal (!!)
- *These:* Geringes Gefährdungspotential bei Diagnostika (Strahlung und Arzneimittelsicherheit)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