Aseptic Processing Barrier Technology Trends with the Use of RABS and Isolators

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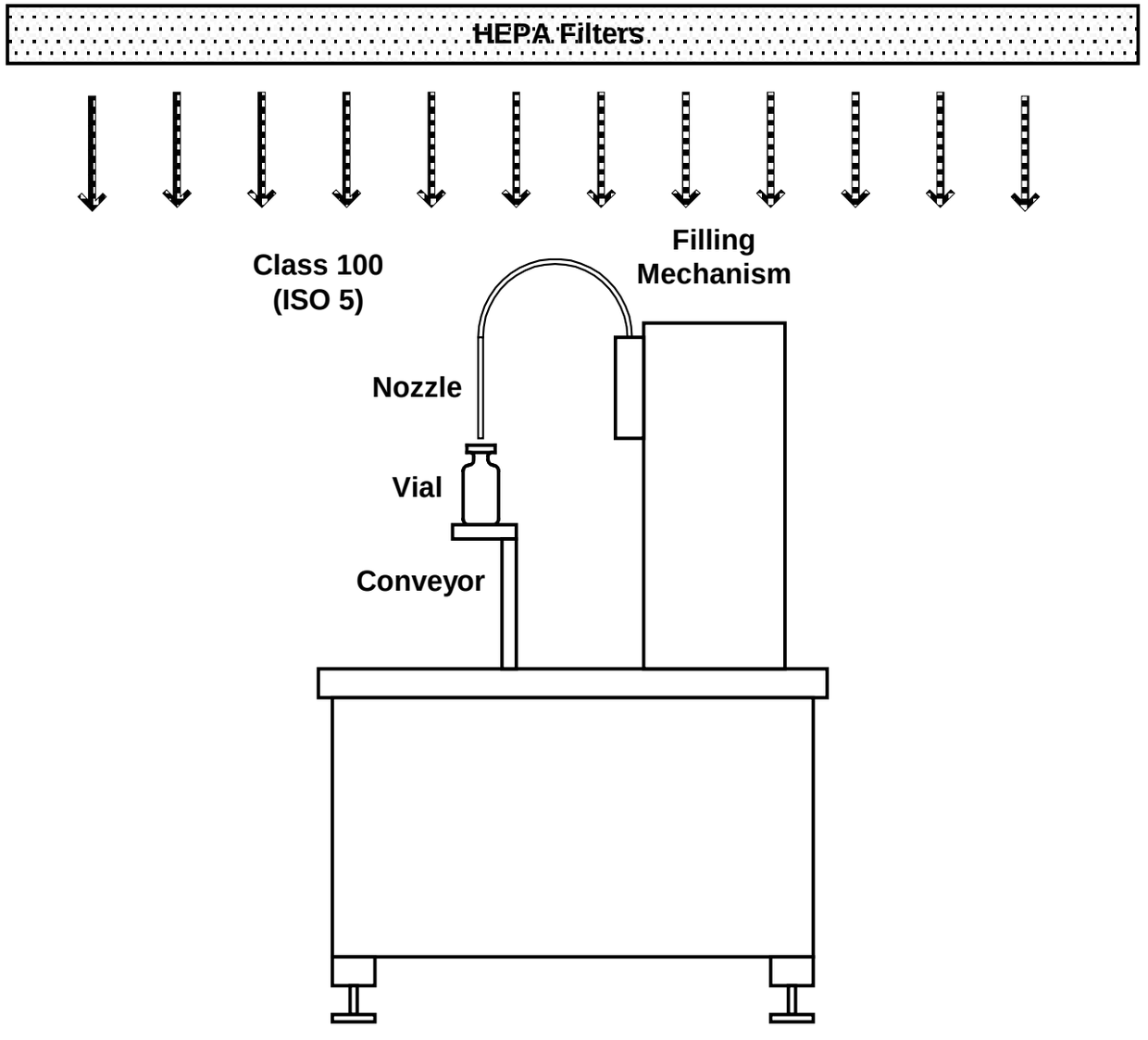
Agenda

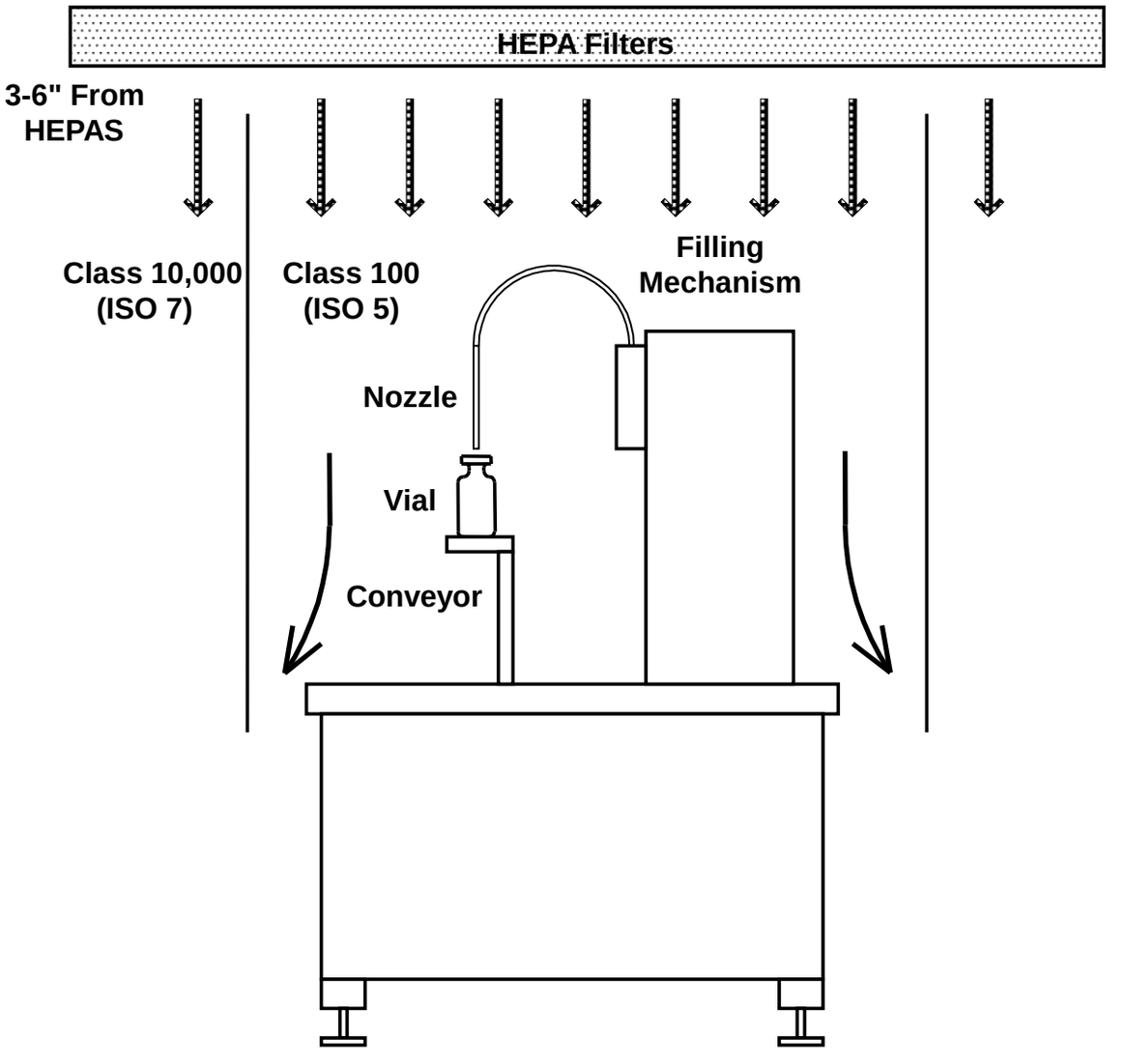
- Background - Diagrams
- Survey Data & Trends
- Q&A

Conventional Clean Room



RABS (Passive)
Restricted Access Barrier System

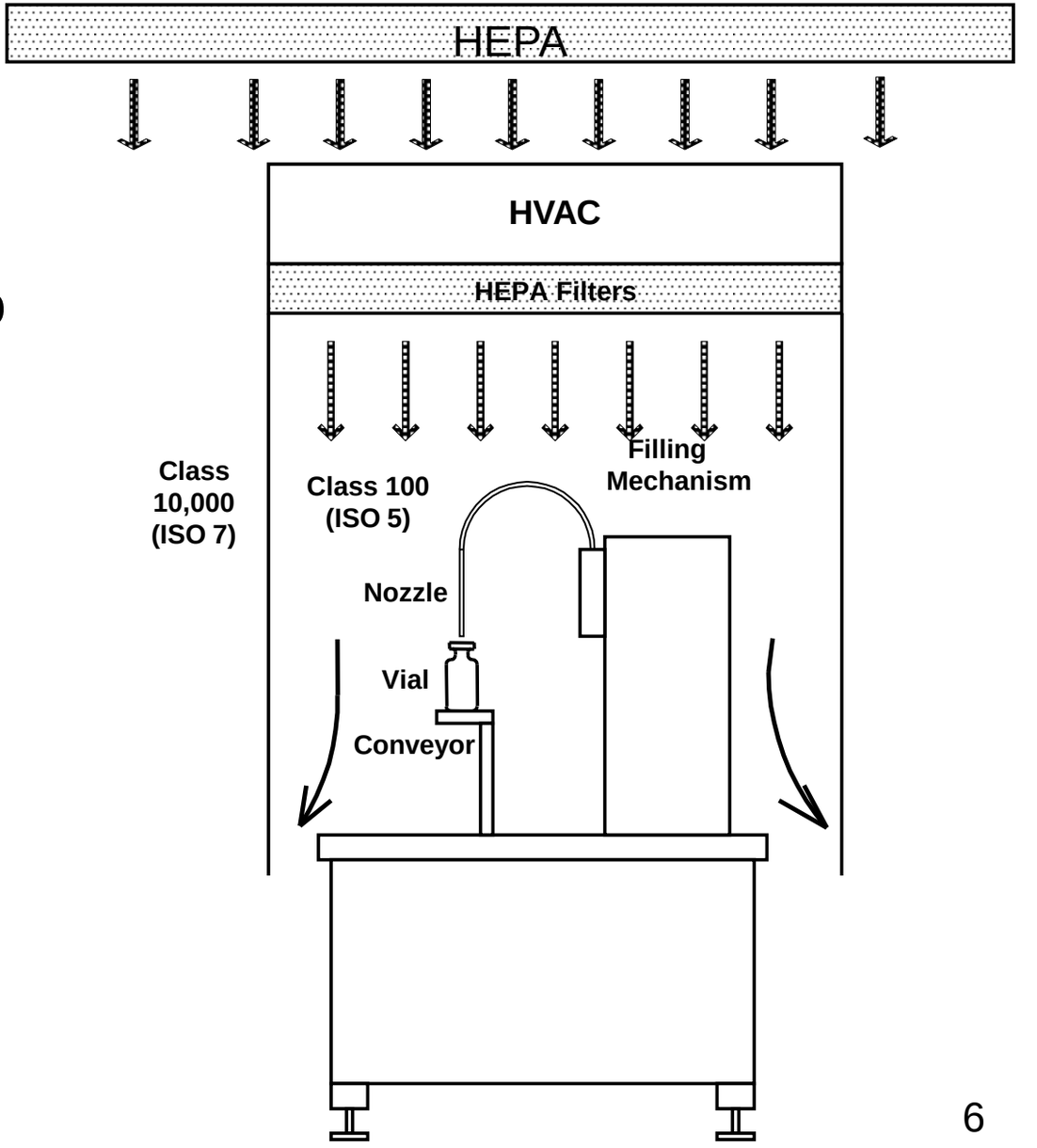
- A barrier to prevent human intervention.
- Air flow provided by ceiling HEPAs to critical zone.
- Bottom of enclosure is open for air outlet.
- Glove ports and Transfer ports used for manipulations and commodity additions.
- Manual high level disinfection.



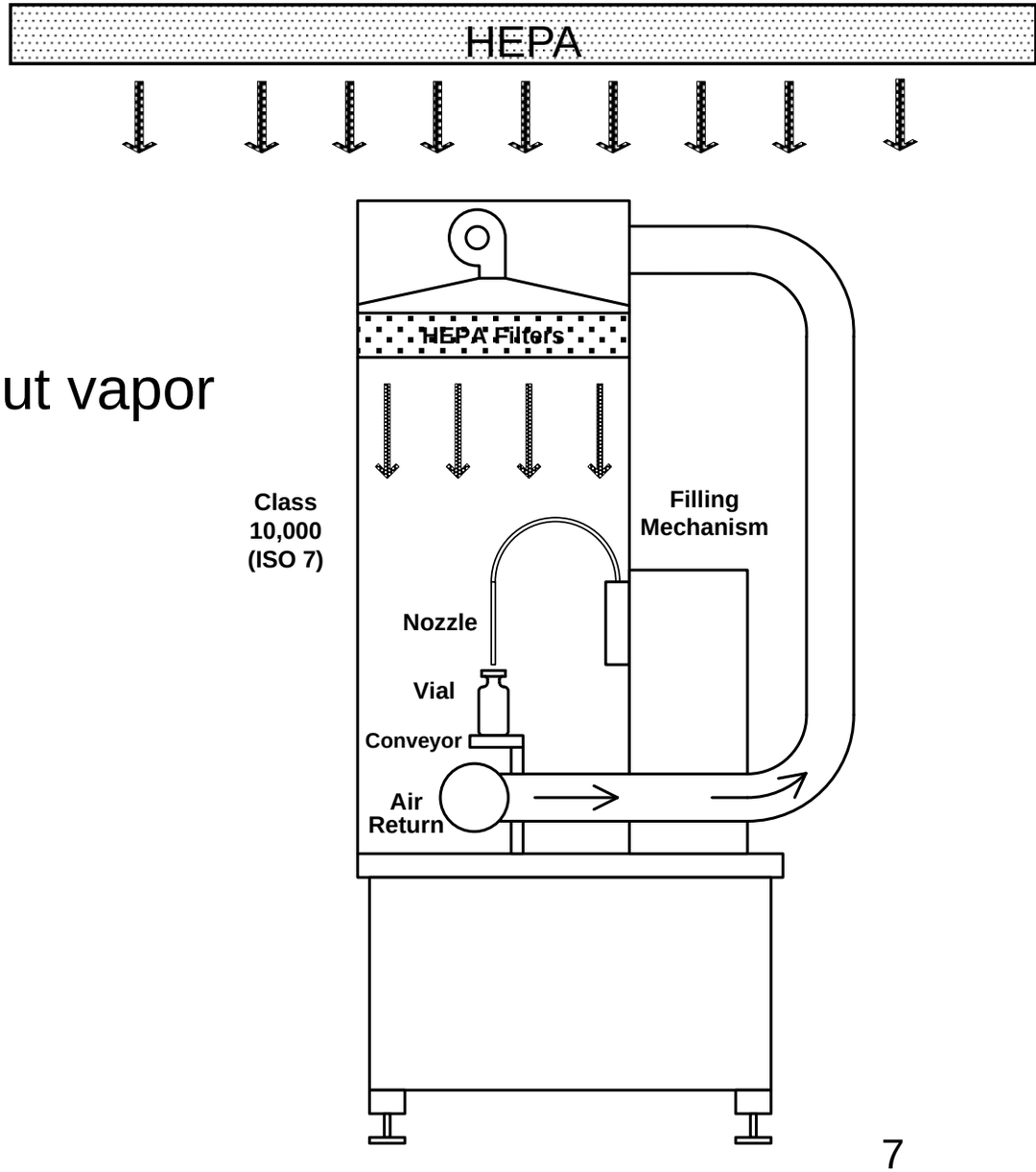
RABS (Active)

Restricted Access Barrier System

- Similar to Passive RABS but with integral HEPA/HVAC air supply to critical zone.
- Easiest way to have flow from critical area to room in case of open door intervention.
- Manual high level disinfection.



- **Closed RABS**
  - •Manual high level disinfection.
  - •Can be Similar to an isolator without vapor biodecontamination.
  - •used for containment applications



RABS needs

- Management Oversight
- A Quality System
- Proper surrounding room design
  - ISO 5 Annex for Open Door routine interventions
- Proper Gowning
- Proper Training cGMP
- Initial high level disinfection with Sporicidal agent
- Proper SOP for rare interventions allowed
- Properly Designed Equipment
- If interventions are allowed (Policy)
  - Disinfection
  - Line Clearance
  - Documentation of event

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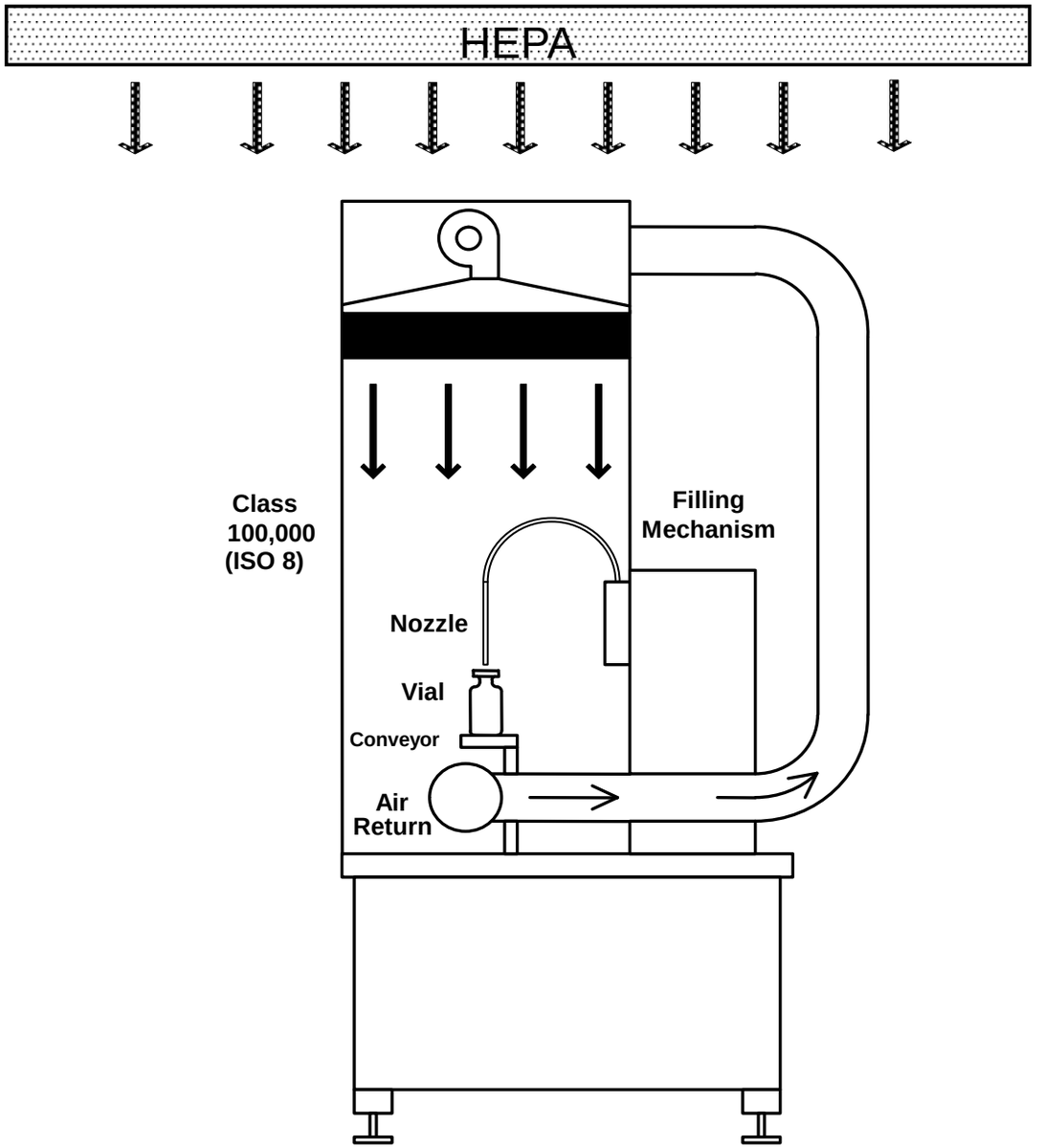
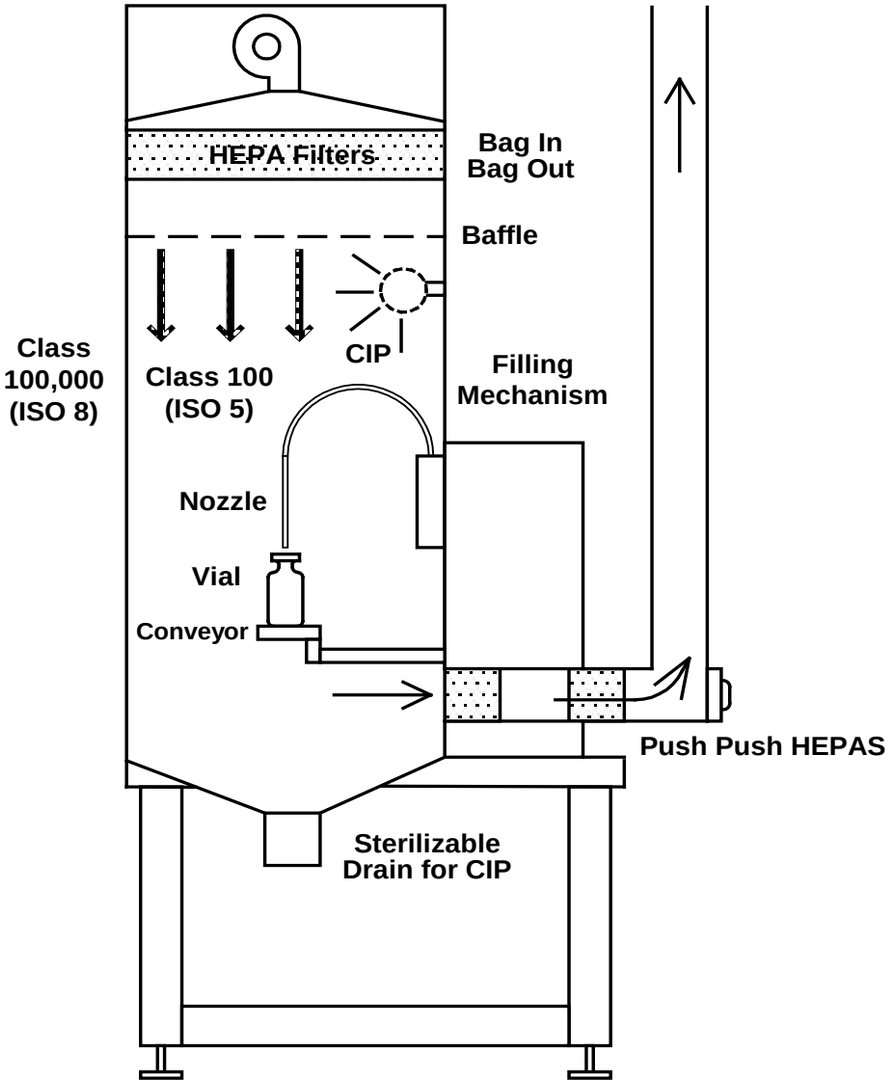
Isolator

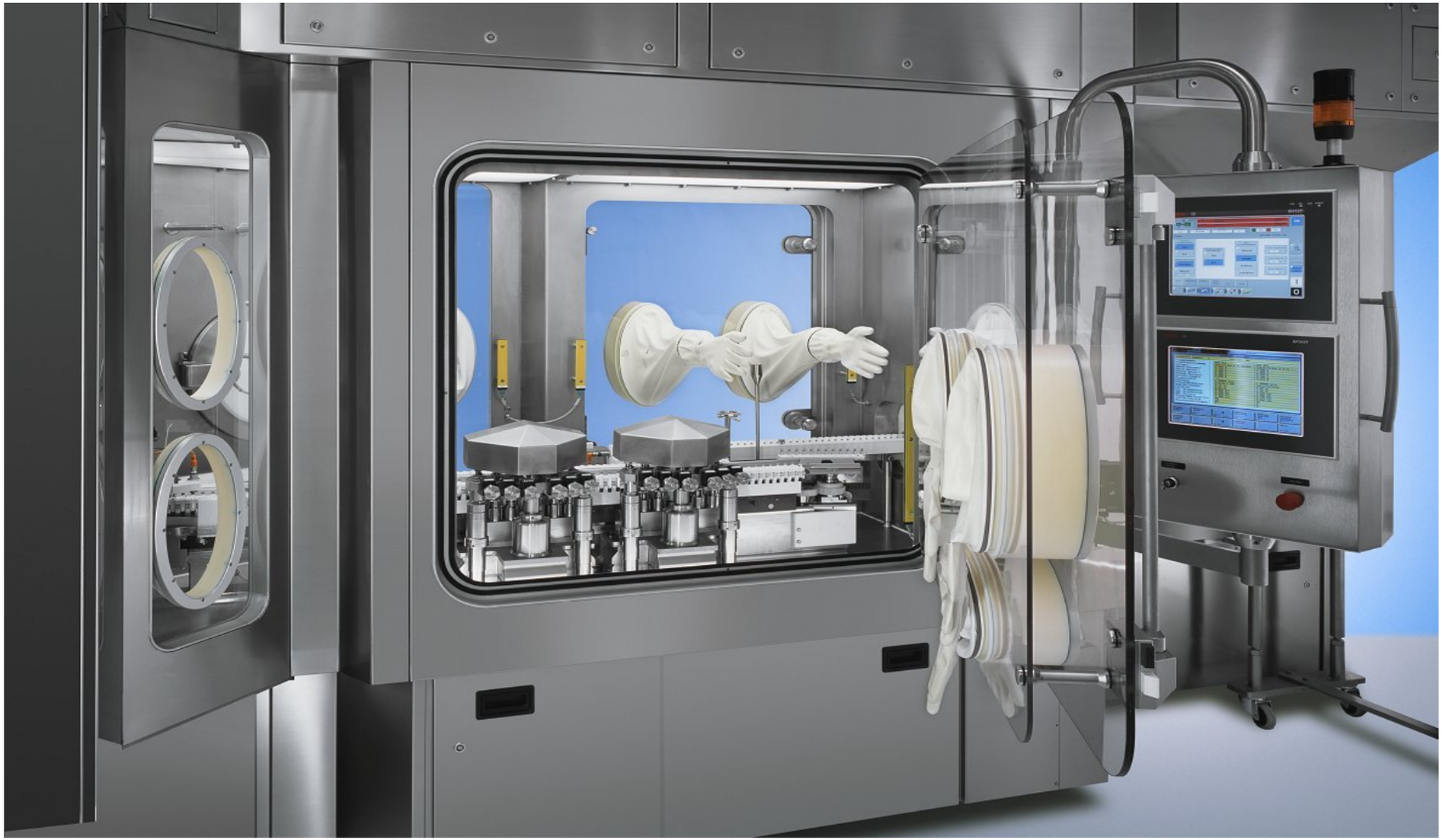

HEPA
Class
100,000
(ISO 8)
Filling
Mechanism
Nozzle
Vial
Conveyor
Air
Return


BOSCH
BOSCH

Isolator for Containment




BOSCH
BOSCH



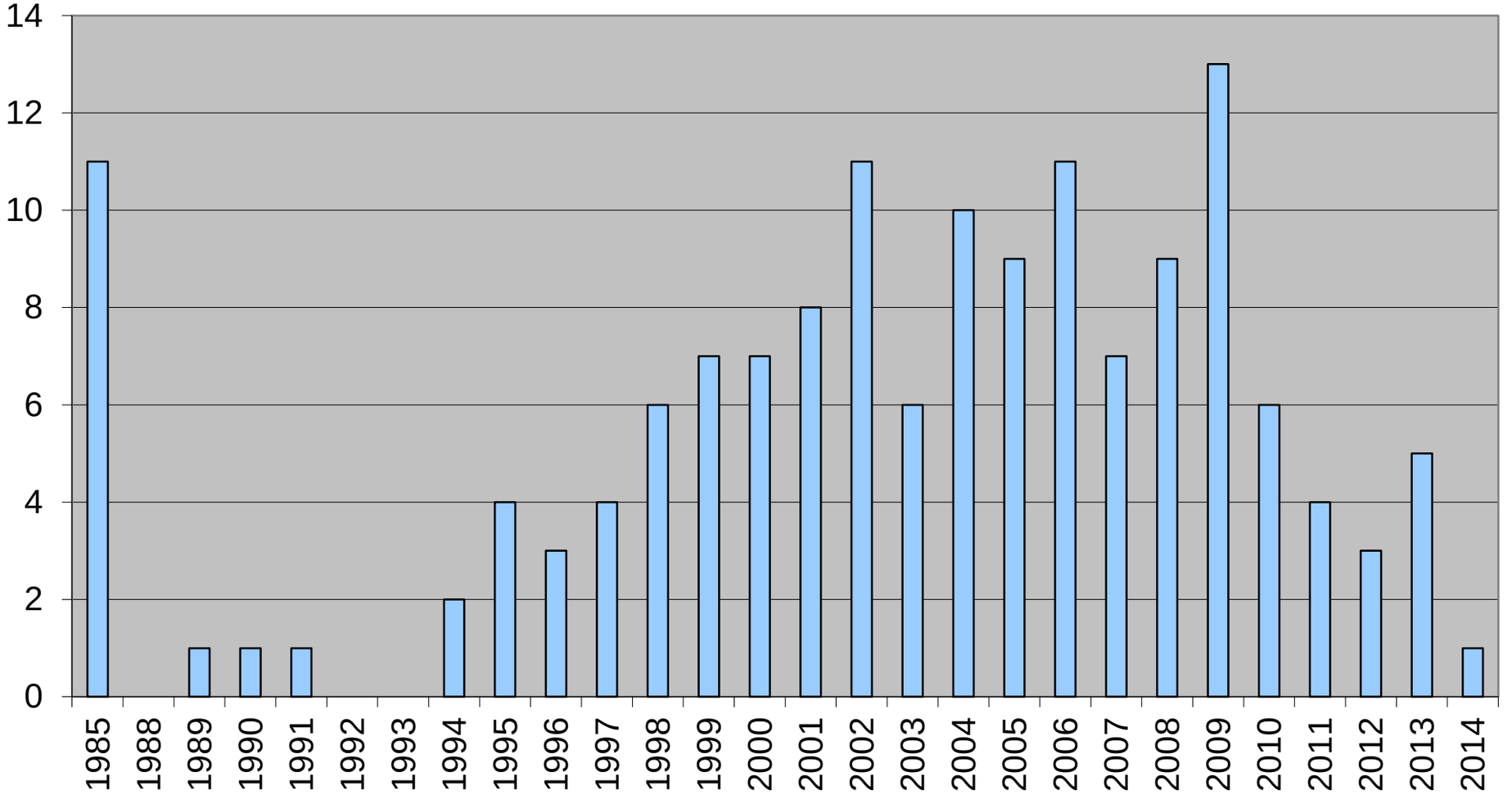
Data & Trends

- Data is from Lysfjord Porter Surveys
- Isolator 1998, 2000, 2002, 2004, 2006, 2008, 2010 and 2012
- RABS 2005, 2007, 2009, and 2011

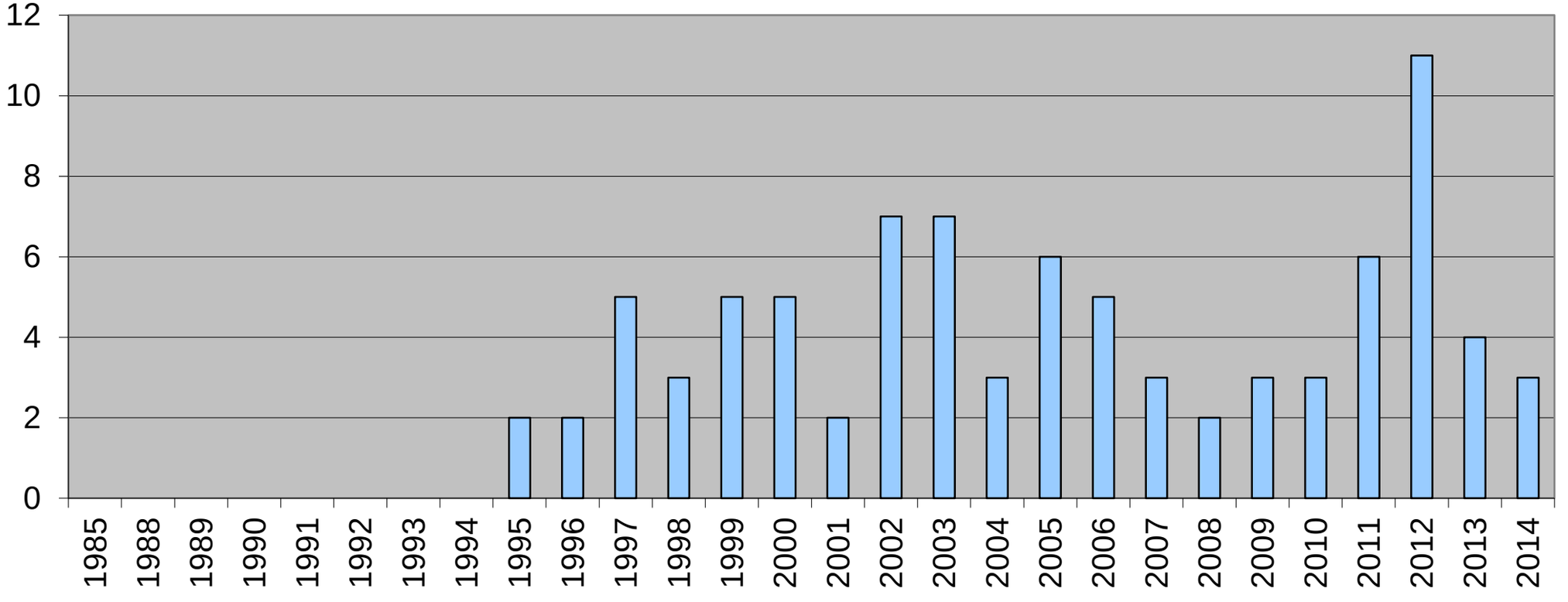
Filling Barriers Survey Summarys World Wide

Year	1998	2000	2002	2004	2005	2006	2007	2008	2009	2010	2011	2012
Isolator	84	172	199	256		304		391		427		490
RABS					75		124		243		378	

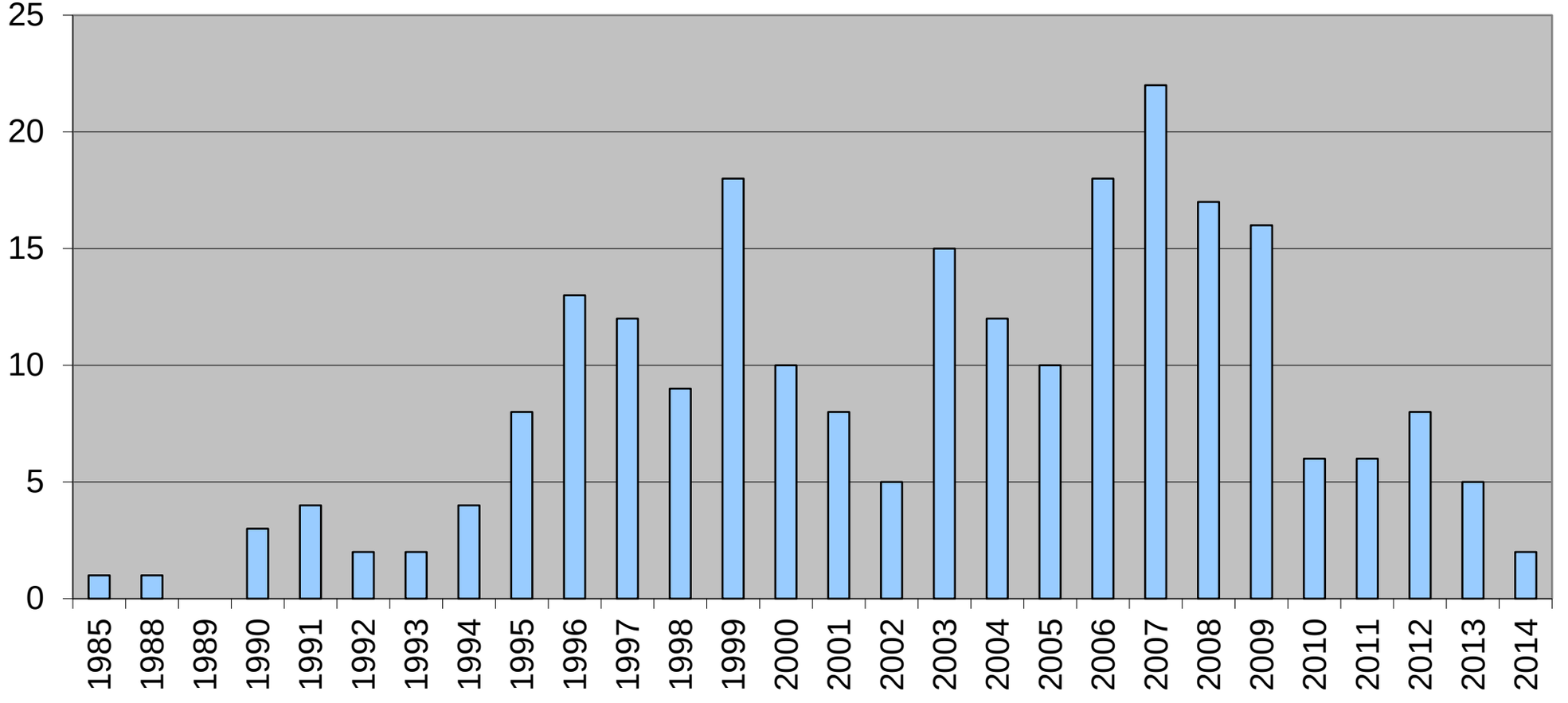
Barrier Isolator Filling Line – Deliveries by Year Total



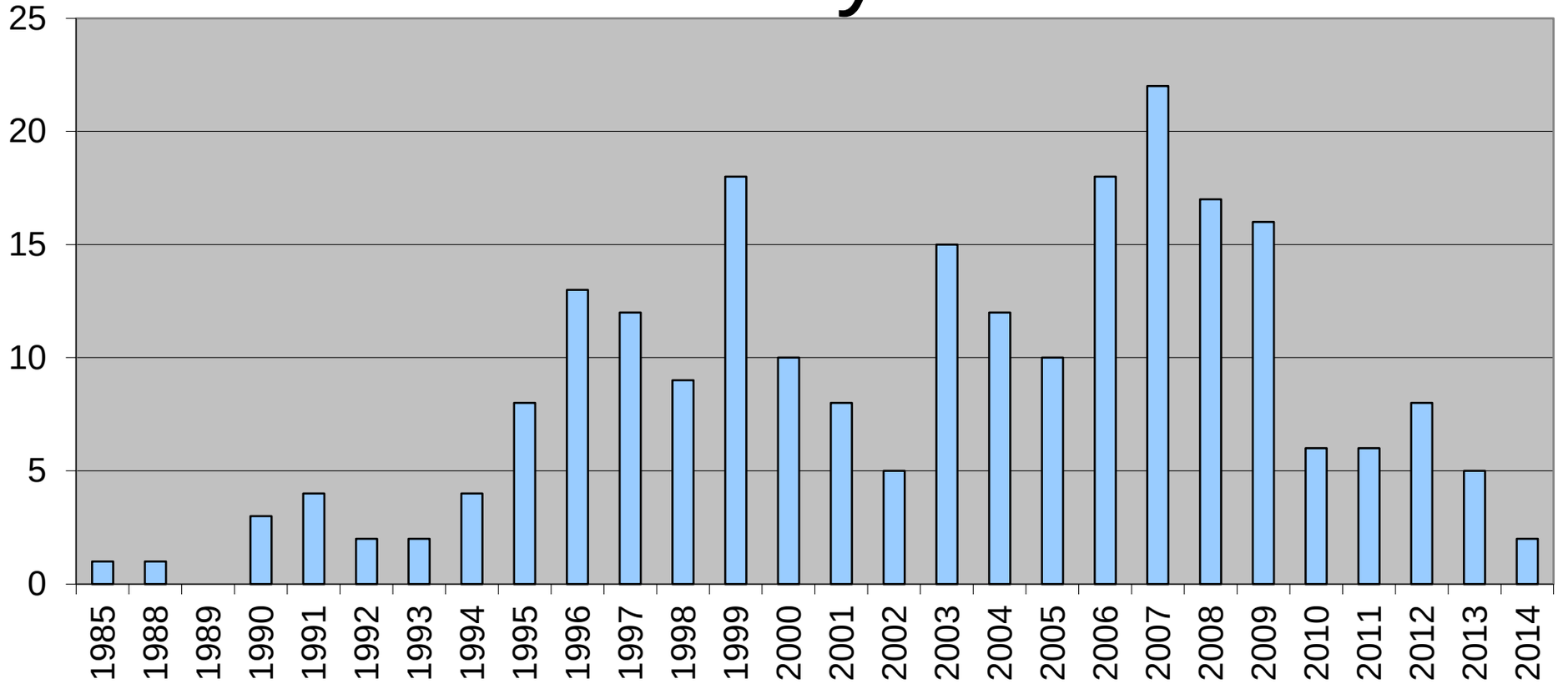
Barrier Isolator Filling Lines – Deliveries by Year - Asia Only



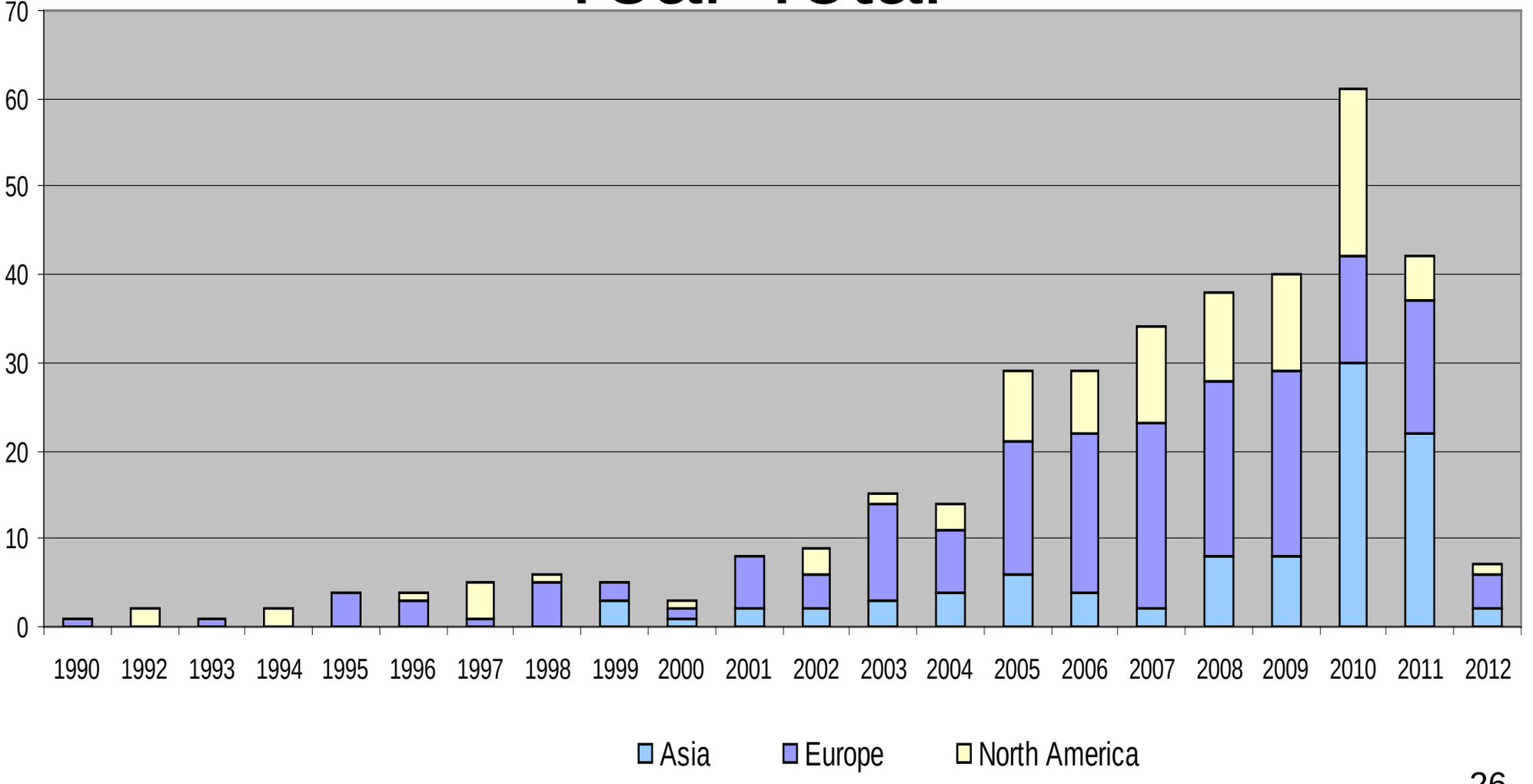
Barrier Isolator Filling Lines – Deliveries by Year - Europe Only



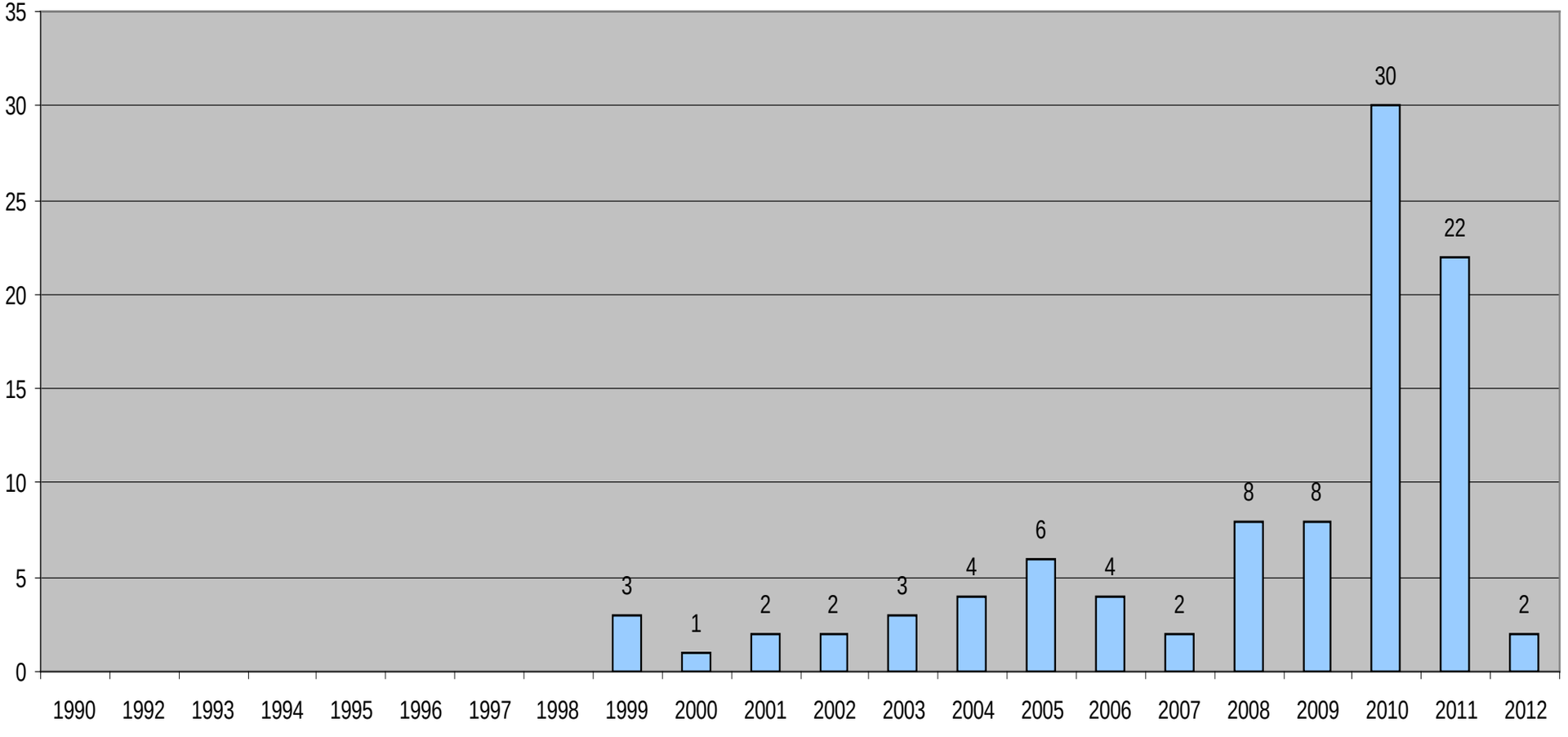
Barrier Isolator Filling Lines – Deliveries by Year - North America Only



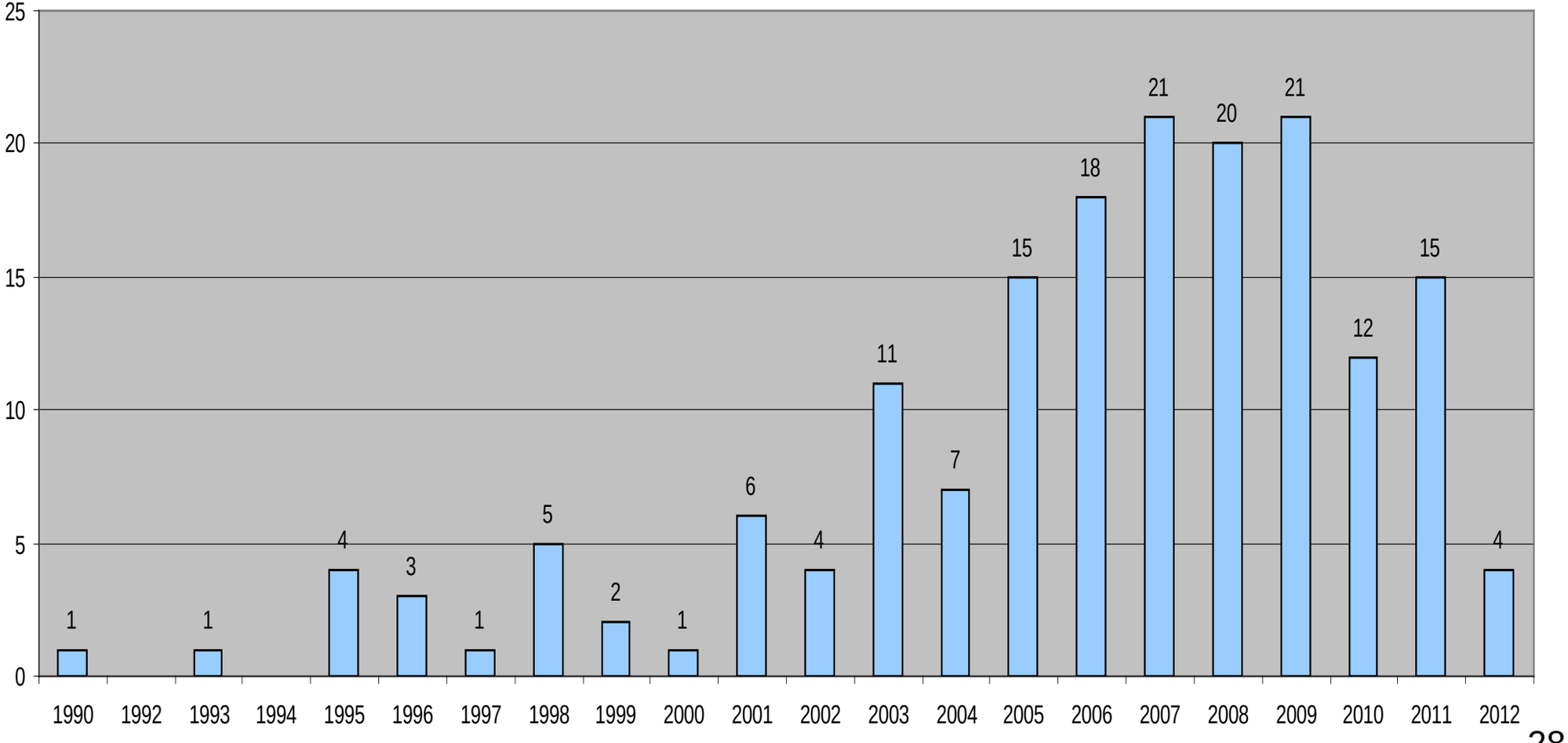
Number of RABS Units Delivered by Year Total



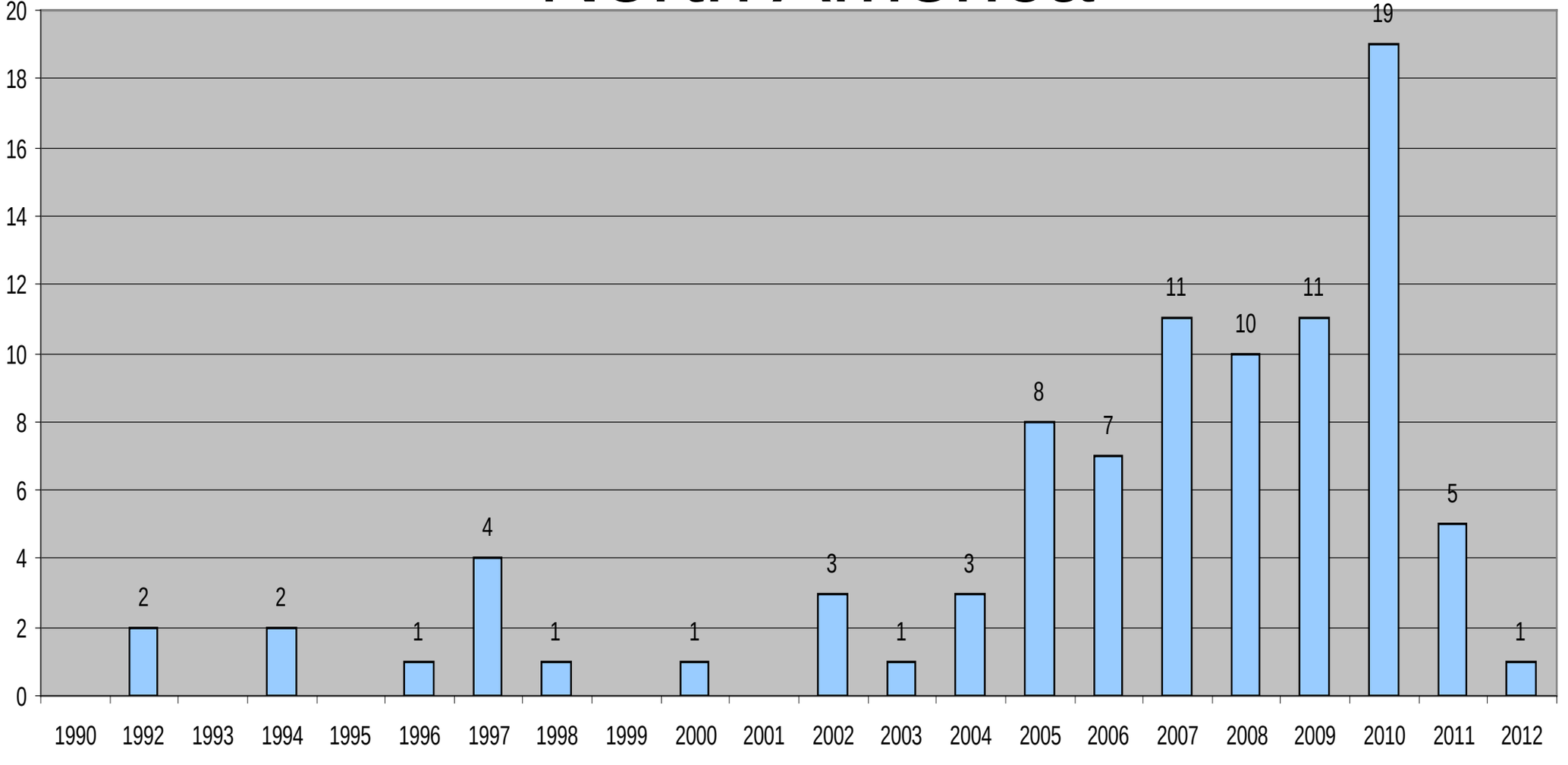
RABS Delivered by Year by Continent - Asia



RABS Delivered by Year by Continent - EUROPE



RABS Delivered by Year by Continent - North America



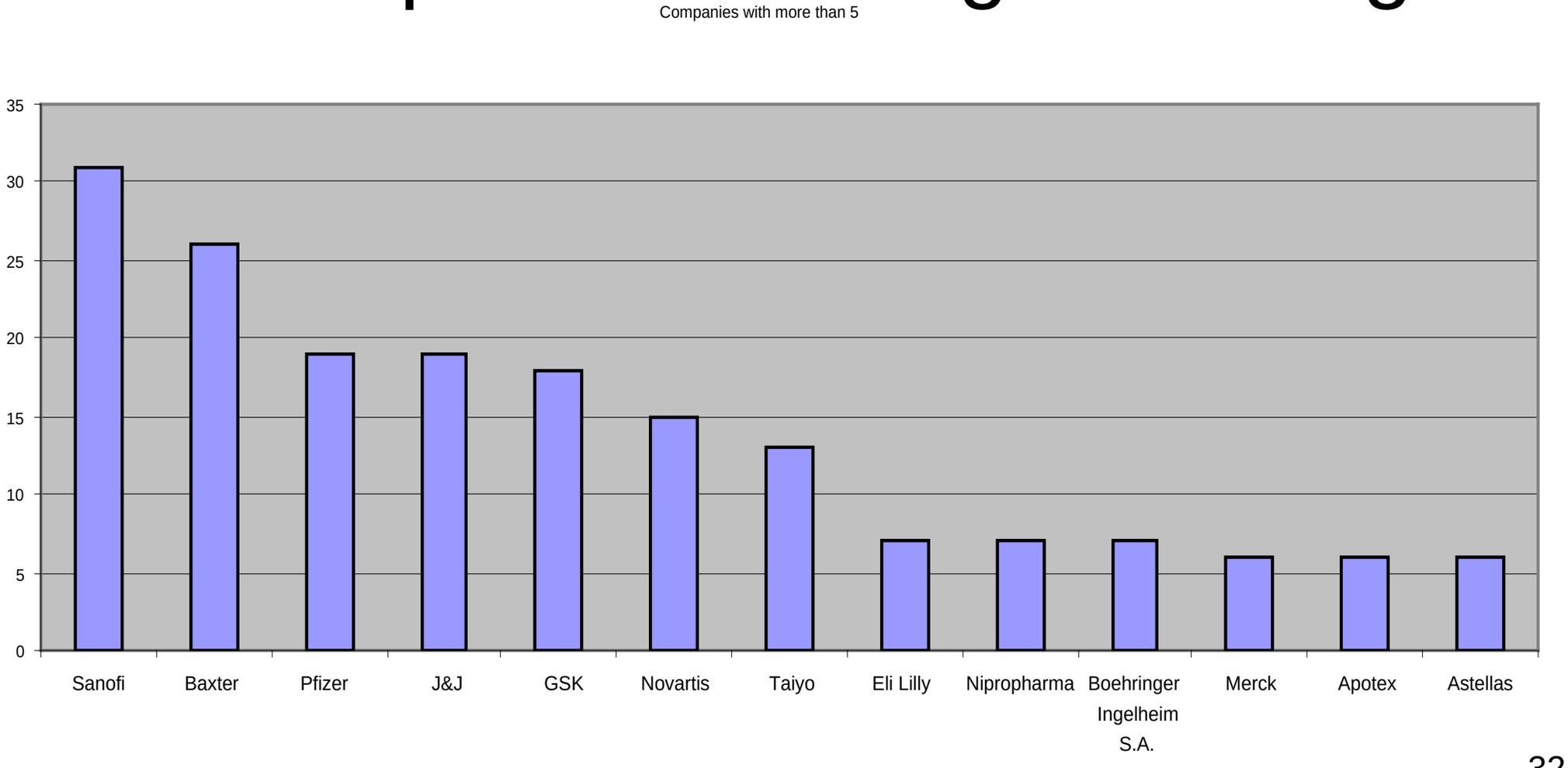
Types of RABS

Year	Passive	Active	Closed	Total
2005	15	25	17	57
2007	19	47	27	93
2009	51	121	64	236
2011	93	198	79	370

Philosophy for Using RABS – DOORS 8% Open Frequently

Year	Never Opened	Limited Open	Frequently Open	Total
2005	23	28	1	52
2007	26	45	6	77
2009	59	87	10	156
2011	89	133	**19**	241

Barrier Isolator Filling Lines Companies with Highest Usage



Top Companies with RABS

	2005		2007		2009		2011	
#	Company	# of RABS	Company	# of RABS	Company	# of RABS	Company	# of RABS
1	Vetter	10	Vetter	10	Pfizer	17	Pfizer	18
2	Pfizer	7	Pfizer	10	Vetter	15	Vetter	18
3	Aventis	5	GSK	7	GSK	12	GSK	18
4	GSK	4	Aventis	5	Merck	11	Merck	18

Container Type Total - Global

	Vial	Ampoule	Syringe /Cartridge	Ophthalmic	IV	Other	Total
2012 Isolator	218	48	99	18	32	19	434
2011 RABS	234	27	77	16	3	9	366

Container Type Asia

	Vial	Ampoule	Syringe/ Cartridge	Ophthalmic	IV	Other	Total
Isolator 2012	29	13	9	6	10	1	68
RABS 2011	20	2	8	7		3	40

Container Type EU

	Vial	Ampoule	Syringe/ Cartridge	Ophthalmic	IV	Other	Total
Isolator 2012	100	28	72	4	1	12	217
RABS 2011	69	13	36	4	2	1	125

Container Type NA

	Vial	Ampoule	Syringe/ Cartridge	Ophthalmic	IV	Other	Total
Isolator 2012	84	7	18	8	21	6	144
RABS 2011	47	4	9	2			62

Reported Number of Lines vs. Maximum Line Speed with Isolator

	1-100	101-200	201-300	301-400	401-500	501-600	601-700	701-800	Total
Total	135	49	65	46	6	16		5	322
Asia	19	4	12	7					42
EU	41	31	37	31	3	10		5	158
NA	74	14	16	6	3	6			119

Reported Number of Lines vs. Maximum Line Speed with RABS

	1-100	101-200	201-300	301-400	401-500	501-600	601-700	701-800	Total
Total	54	76	47	64	16	10			267
Asia	4	25	4	7	7	1			48
EU	33	37	36	34	8	5			153
NA	18	15	14	9	6	4			66

Gloves

- 2nd Disposable Glove Used; Isolator 89% Yes, RABS 98% Yes
- Testing by Visual Inspection and Pressure Decay is Predominant Test for Both Isolator and RABS
- Replacement up to 6 months with “As Needed” most prevalent for Both Isolator & RABS
- 1 Piece 46%, 2 Piece 54%*
- Smooth Sleeve 85%, Pleats 15%*
- * Isolator data only

Containment

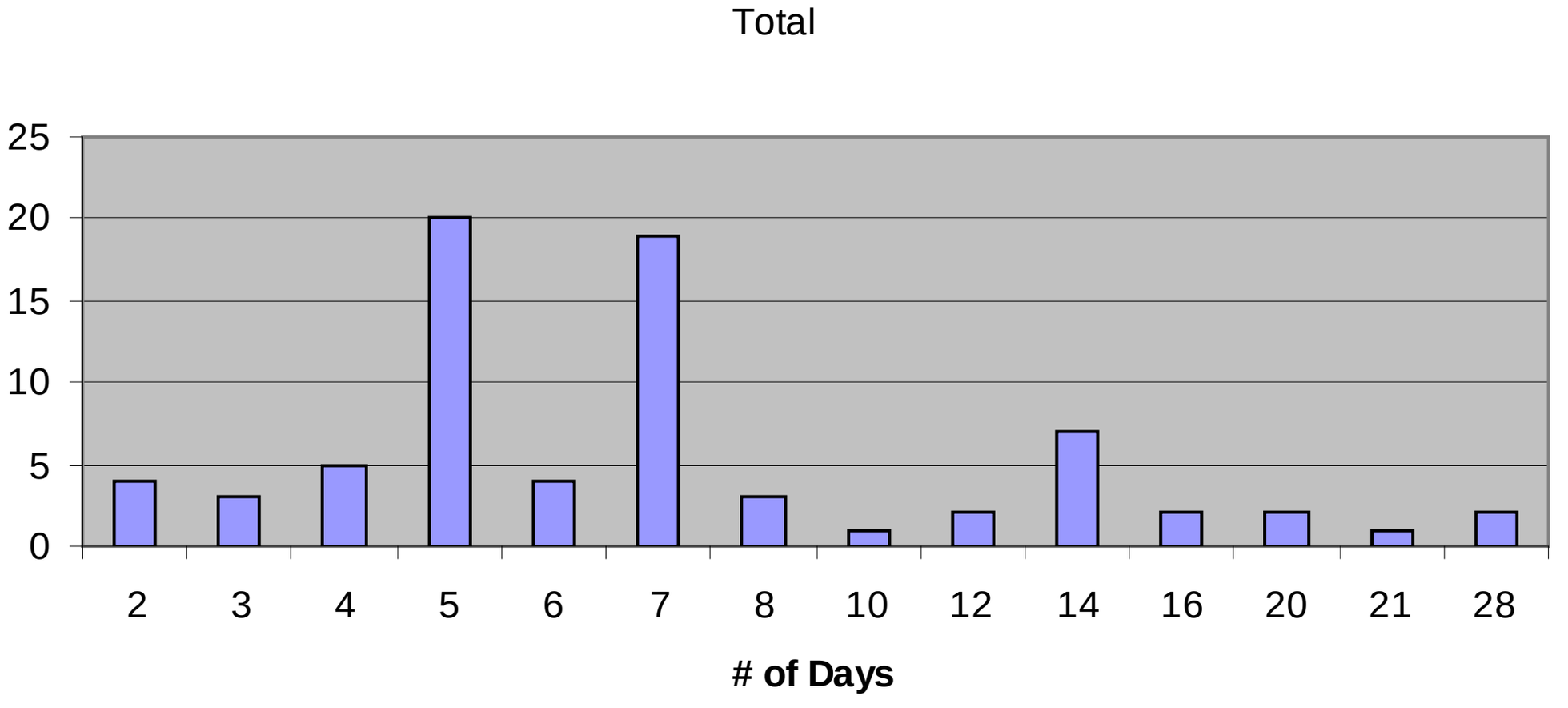
- Isolator, 108/228 Need Containment = 45%
- RABS, 16 Indicated a Containment Need

Do you Campaign Products (Isolator) (run for multiple days)?

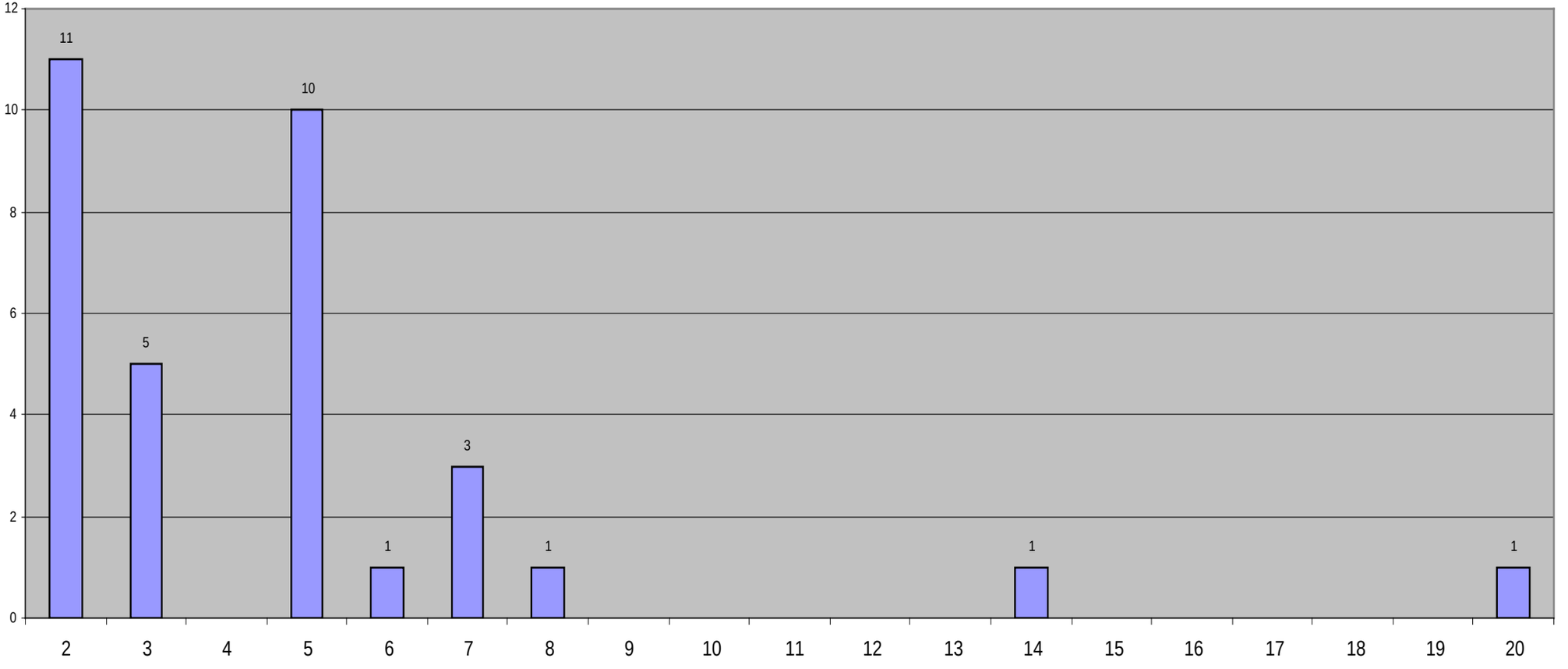
No	51	35% of Total
Yes	94	65% of Total*
Total	145	

***65% was 51% in 2006 data**

Campaign Products (longest run, Isolators)



Number of Days Line Campaigned RABS



Trends

- Both Isolator and RABS Use Is Increasing
- Syringe in Tubs Is Rapidly Increasing in EU Isolator
- Containment Need is Increasing Especially with Isolator
- 94% of Isolators Use H2O2 As a Biodecontaminant
- Campaigning Use and Duration Are Both Increasing 28 days Isolator, 20 days RABS

Trends Continued

- Data Is Harder to Get
- RABS Problem; To Mount Sterile Stopper Feed Components Aseptically! Trend in EU (Bioquell and Steris), NA (Steris) and in Japan (Airex, JGC and Shibuya) Is to H2O2 Room with RABS and get 6 Log Reduction of Bioburden on Stopper Feed Parts
- RABS Problem; 8% of Doors Are Opened Frequently- Regulatory Issue!
- Jump in Rate of Deliveries for RABS 2009-2011 Due to Annex 1 Capping Change and CMO Retrofits on Existing Lines

Trends Continued

- So Which Best? Isolator or RABS?
- It Depends, on Application Needs.
- Both are Tools That Work, IF Used Properly.
- Keep Doors Closed on RABS.

Thank You!

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