5-8-2018

Cell Culture Bioprocess Learnings: Past successes and future challenges

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Cell Culture Bioprocess Learnings

– ten thought provoking views

Günter Jagschies, GE Healthcare Life Sciences

BioProcess Capability Days Japan

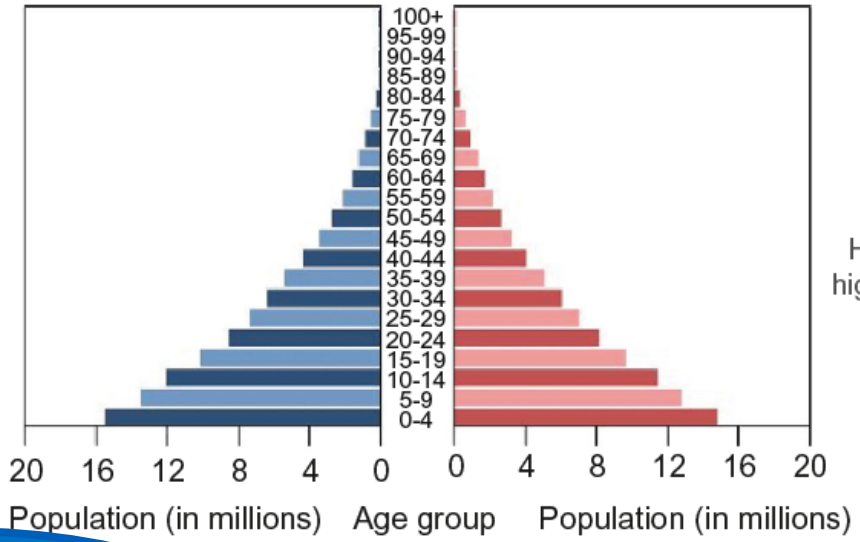
2018-June 27

Please contact me at guenter.jagschies@ge.com in order to request a complete copy of my keynote presentation at CCE in Tampa

With permission: G Jagschies et al., “Biopharmaceutical Processing: Development, Design, and Implementation of Manufacturing Processes”, Elsevier 2018

#1 - Health challenge transition

Demographic transition (blue = male, red = female)

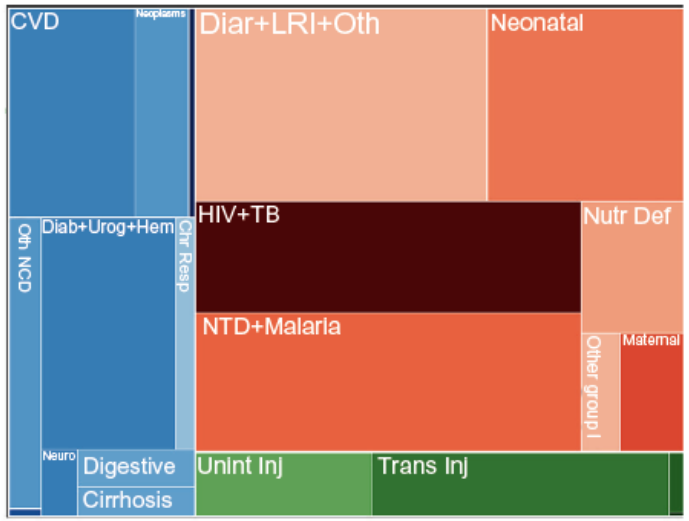


Nigeria
Juvenile

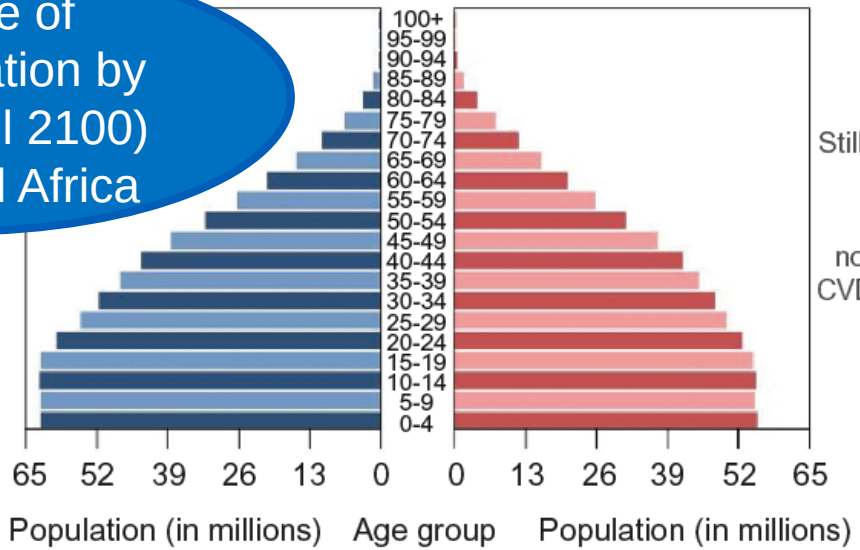
Dominating communicable disease

Hygiene, access to care: high newborn and maternal mortality

Unsafe life conditions



Increase of >65 population by 2.3 bn (until 2100) in Asia and Africa

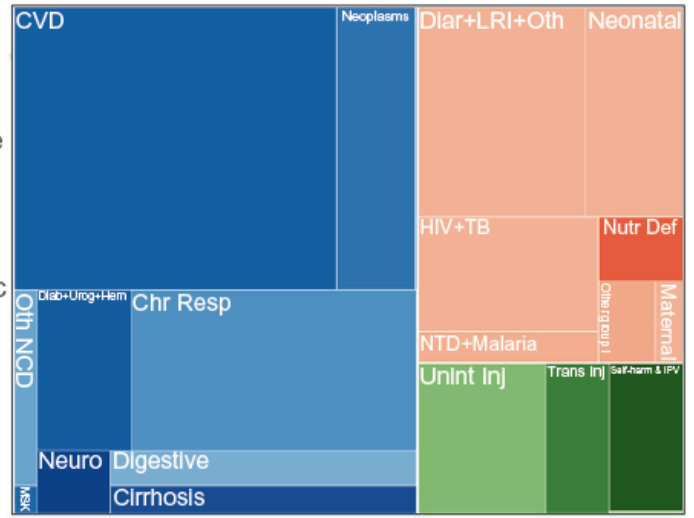


India
Young

Still significant communicable disease burden

Sharply growing noncommunicable disease: CVD, cancer, diabetes, chronic respiratory disease

Unsafe life conditions



Graphs used with permission from Institute for Health Metrics and Evaluation (IHME), GBD Compare. Seattle, WA: IHME, University of Washington, 2016
Available from http://vizhub.healthdata.org/gbd-compare/. (Accessed January 2017.)

#4 - Beyond antibodies
Time to simplify and to integrate

Innovations in therapeutic molecules

Antibody drug conjugates
Bi-specific mAbs
Fragments
Nucleic acids
Scaffolds
Gene therapies
Cell therapies
mRNA

Biomanufacturing toolbox

Flexible unit operations, multi-molecule capable

HTPD*, QbD*, PAT*

Integration

Continuous processing

Automation, data integration, digitalization

Modularity, wheel in-wheel out equipment

SUT* standards
E&L* service standards

Facility design

Minimal foot print
Right-sized, scale out

Minimal piping
smaller & less tanks

Simplification

Single-use technology

Digitalization
Less complex equipment, no bespoke solutions

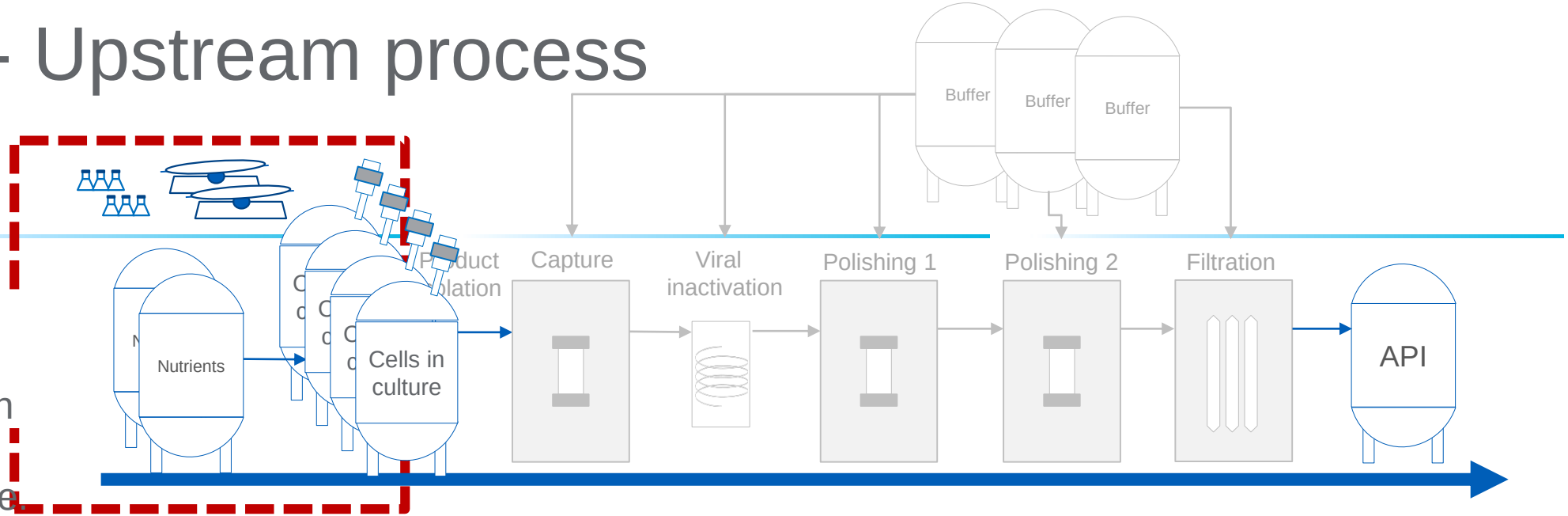
In- and at-line analytics

Matching demand increase or new market entry

*E&L = extractables and leachables, HTPD = high-throughput process development, PAT = process analytics technology, QbD = quality by design, SUT = single-use technologies

#5 - Upstream process

Each step in the process can be operated in batch or continuous mode.



Cell line development (CLD)

- **Reduction of CLD time from 40 weeks (traditional) to 10 weeks**
- **Less screening:** more projects, more time for difficult to express proteins
- **Product quality**, not just titer !!!

Cell culture, batch

- **Titers reach** or exceed **10 g/L**
- **Advanced** approaches to boost viable cell density
- **Fine tuning ”nutrition”**
- **Time compression** for inoculation train and production reactor

Cell culture, perfusion

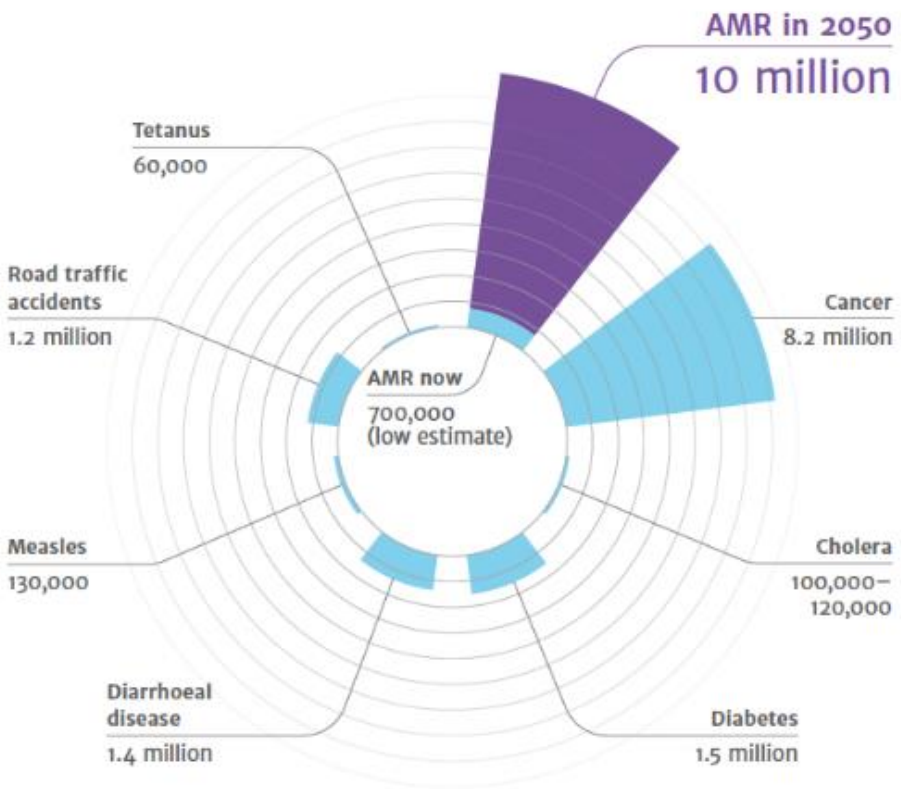
- **Foot print reduction ~50%** (5-10 fold vol reduction)
- Elevated **volumetric productivity** (3-5 g/L/day) and **reduced perfusion rate** (0.2-0.5 RV/day)
- **Mitigate perceived or real business risks** via simplification (e.g., iSKID)

#10 - Disease challenges far from solved

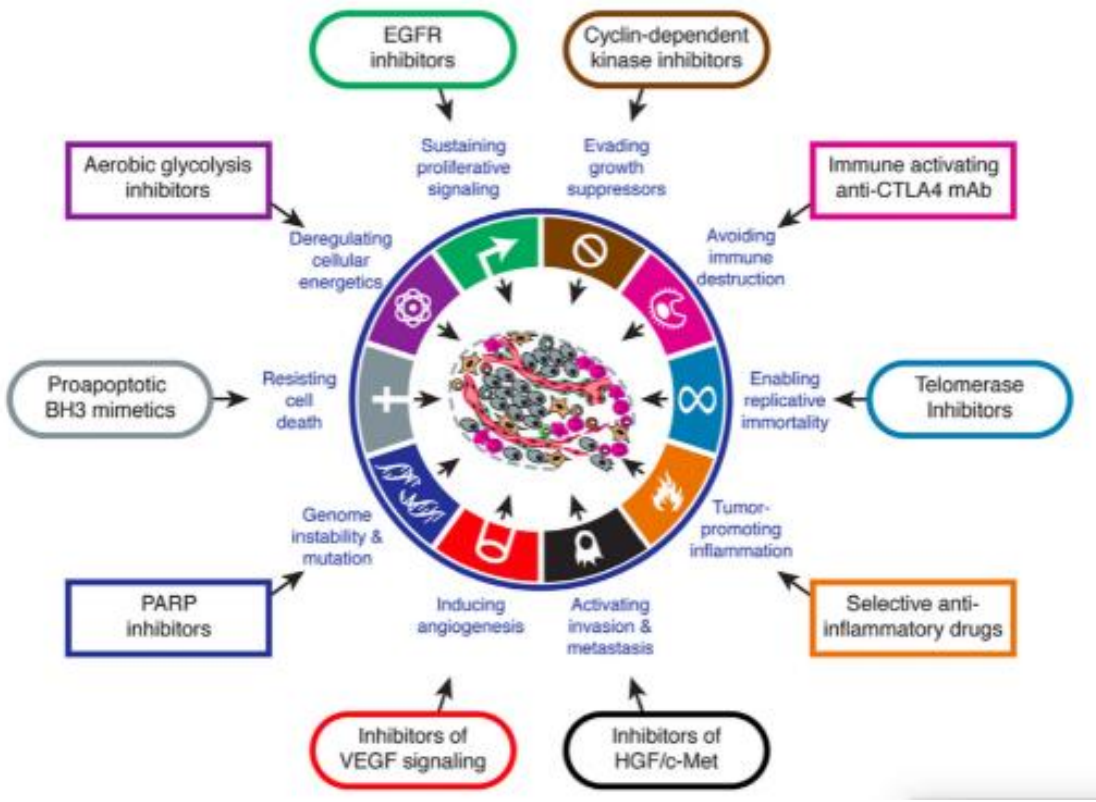
Unlikely for any company to address these challenges alone!

Alzheimer's disease
Parkinson
Tuberculosis
Malaria
HIV

Lose against antimicrobial resistance?



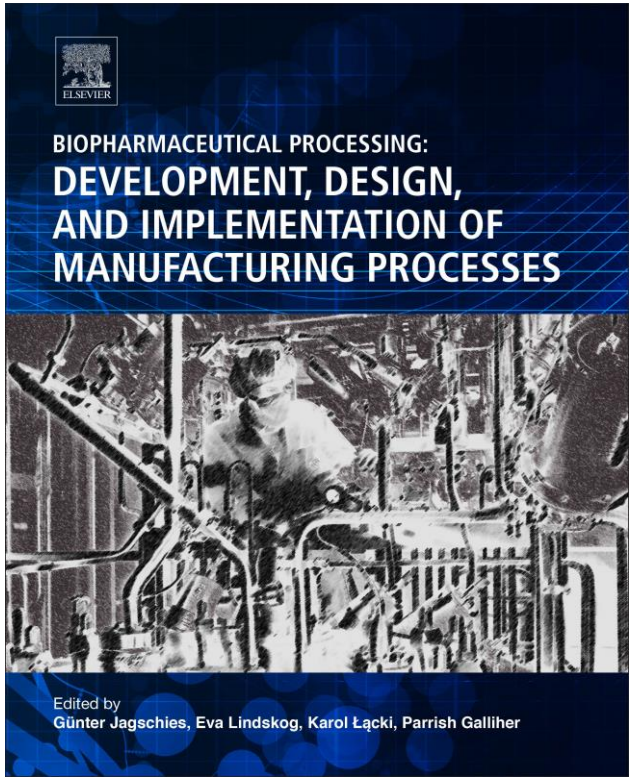
Win over cancer?



Biotherapeutics for the most complex diseases we know, such as cancer or diseases of the nervous system, are still in the earlier phases of their efficacy and potency related "learning curves." Consequently, additional generations of biotherapeutics will have to be developed before one may hope for victory over those diseases or even for regularly bringing patients back to a status where life with the disease is long-term manageable.

Biopharmaceutical Processing (just published)

Günter Jagschies, Eva Lindskog, Parrish Galliher and Karol Łącki



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58 chapters covering

- ✓Disease priorities
- ✓Biopharma business
- ✓Process capabilities & designs
- ✓Principles & Methods
- ✓Equipment & Facilities
- ✓Analytics, Quality, CMC
- ✓Industry case studies
- ✓Economics of bioprocessing

100 authors, 1.200 pages