



Translating **science**
into **global** health impact

TB Vaccine Development Pathway

DCVMN - Webinar

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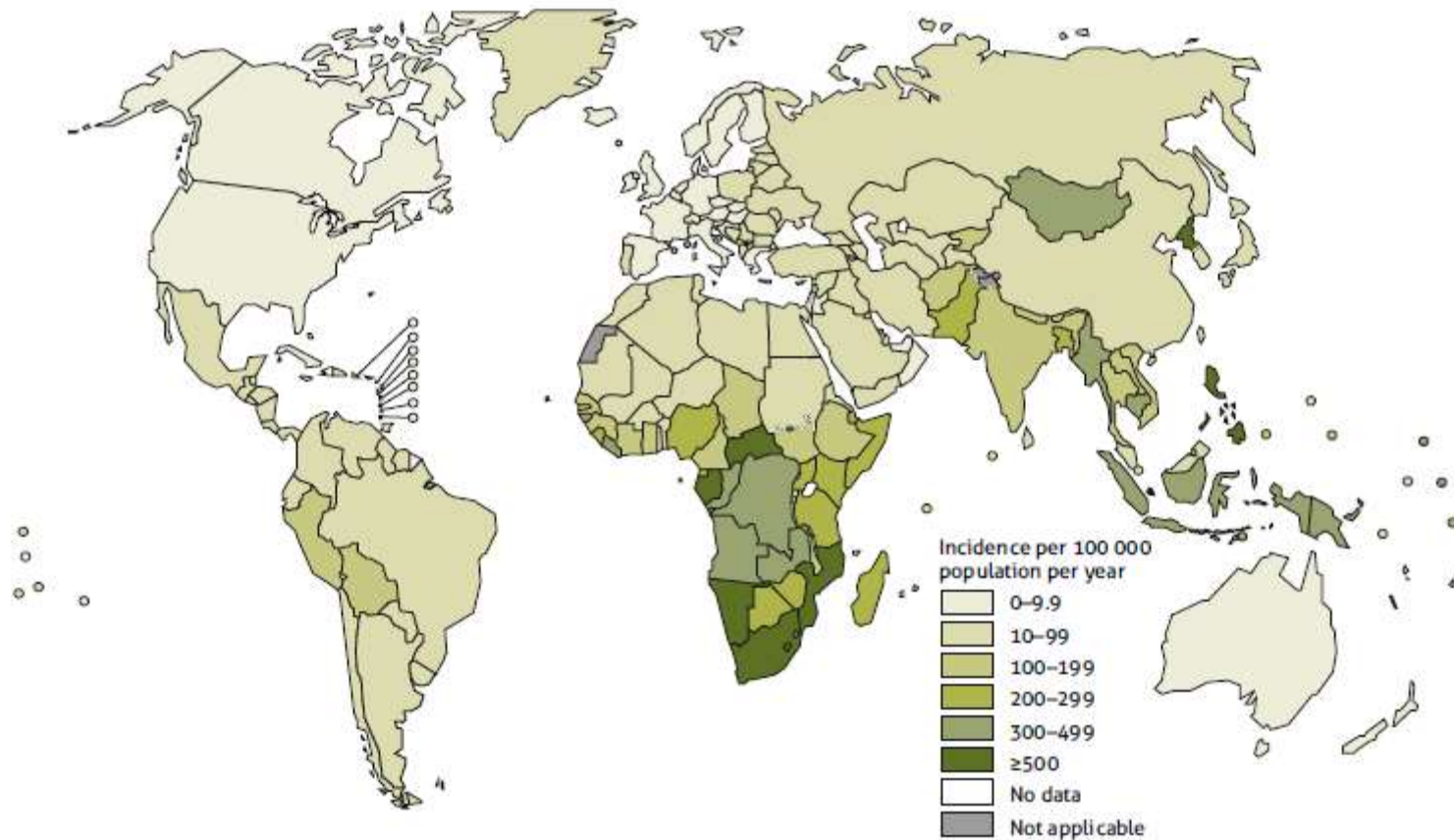
Mycobacterium tuberculosis

In 2018,

- 10.0 million people ill from tuberculosis (TB)
 - 1.1 million children
- 1.5 million people died
 - 205,000 children
 - 251,000 HIV+
- 484,000 new cases of rifampicin-resistant TB, of which 78% were multidrug-resistant
- Geographically, cases were for 44% in South East Asia, 24% in Africa and 18% in Western Pacific

WHO Global Tuberculosis Report 2019

Tuberculosis, incidence rate, 2018

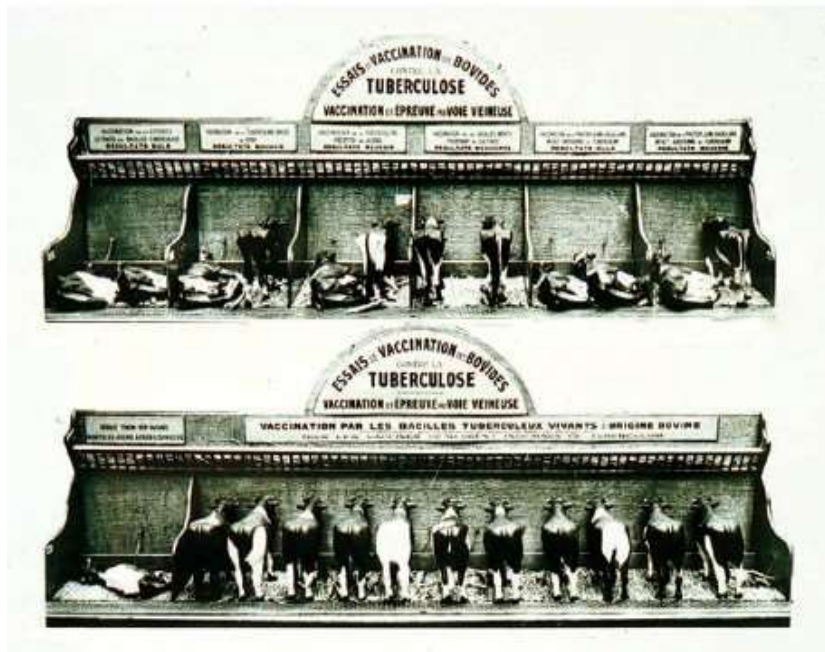


WHO Global Tuberculosis Report 2019

BCG, a widely used vaccine

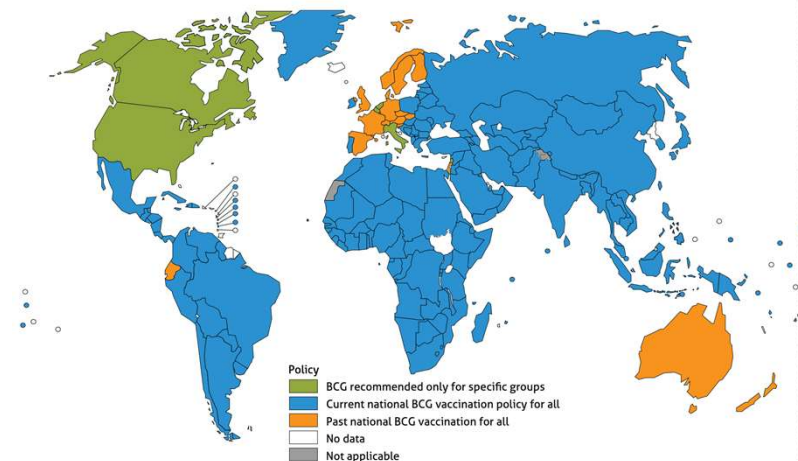
BCG, Bacillus Calmette-Guérin:

- Attenuated *M. bovis*; only TB vaccine licensed (1921), widely used
- Efficacious against severe TB disease in children, though variable protection in adolescents and adults, and safety considerations in HIV-infected infants / children

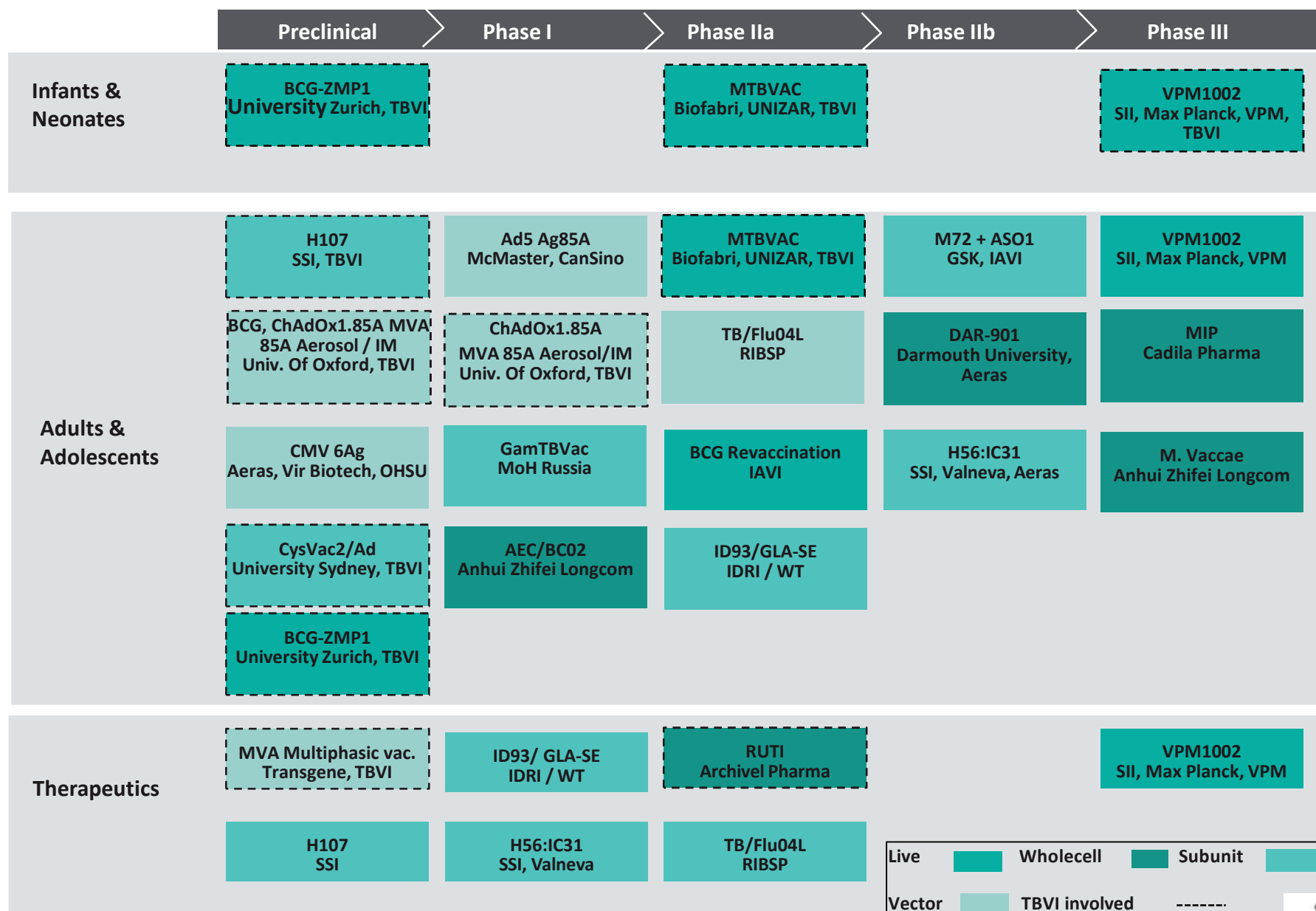


C. Loch, 2017. History of BCG; WHO Global Tuberculosis Report 2019

BCG vaccination policy by country



New vaccines are needed to end TB



From Voss et al, 2018, Progress and challenges in TB vaccine development. F1000 Research

Promising data...

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prevention of *M. tuberculosis* Infection with H4:IC31 Vaccine or BCG Revaccination

E. Nemes, H. Geldenhuys, V. Rozot, K.T. Rutkowski, F. Ratangee, N. Bilek, S. Mabwe, L. Makhethhe, M. Erasmus, A. Toefy, H. Mulenga, W.A. Hanekom, S.G. Self, L.-G. Bekker, R. Ryall,* S. Gurunathan, C.A. DiazGranados, P. Andersen, I. Kromann, T. Evans, R.D. Ellis, B. Landry, D.A. Hokey, R. Hopkins, A.M. Ginsberg, T.J. Scriba, and M. Hatherill, for the C-040-404 Study Team†

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 2b Controlled Trial of M72/AS01_E Vaccine to Prevent Tuberculosis

O. Van Der Meeren, M. Hatherill, V. Nduba, R.J. Wilkinson, M. Muyoyeta, E. Van Brakel, H.M. Ayles, G. Henostroza, F. Thienemann, T.J. Scriba, A. Diacon, G.L. Blatner, M.-A. Demoitie, M. Tameris, M. Malahleha, J.C. Innes, E. Hellström, N. Martinson, T. Singh, E.J. Akite, A. Khatoon Azam, A. Bollaerts, A.M. Ginsberg, T.G. Evans, P. Gillard, and D.R. Tait

- *Nemes et al, 2018*
- *Van Der Meeren et al, 2019*

The Stage-Gate Pathway

- Initiated in 2010 by TBVI and AERAS (now IAVI) with the aims :
 - to provide TB vaccine developers a body of knowledge and a data-driven methodology that standardizes the development of any TB vaccine
 - to provide the TB scientific community, funders and decision-makers rational criteria for assessment of candidates and accelerate progression of the most promising
 - to manage and sustain the pipeline with balanced investment
- First published in 2012*
- Revised in 2017, on internet in 2018 as *'TB Vaccine Development Pathway - a tool to accelerate progression of TB vaccine candidates'*, revised in 2019.

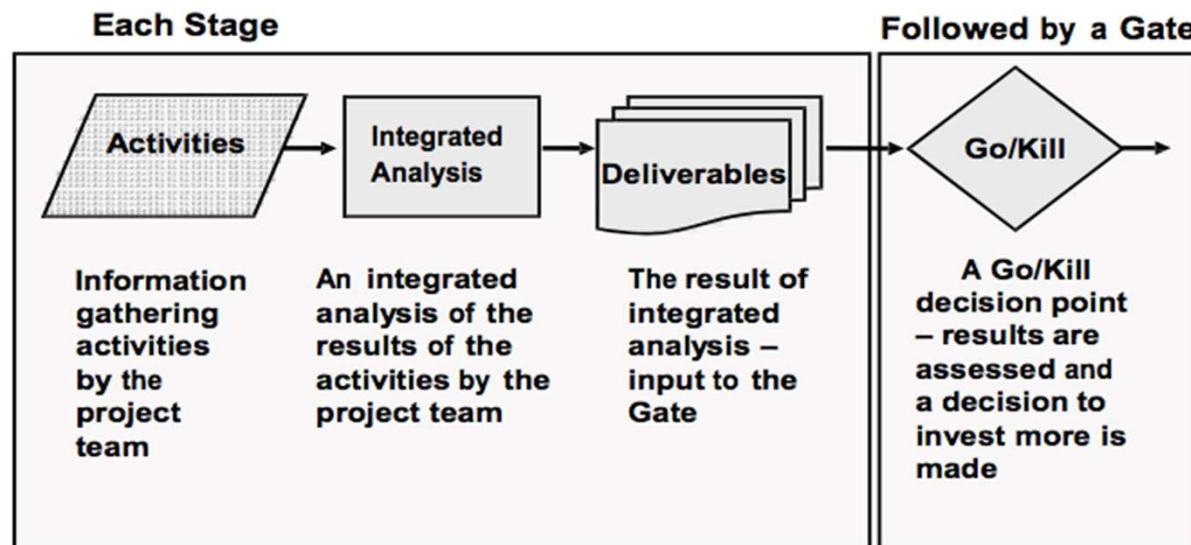
*: Barker et al, 2012. Rational approach to selection and clinical development of TB vaccine candidates, in *Tuberculosis*

What is a 'Stage-Gate' ?

Stage-Gate * is a project management methodology that divides large projects into:

- segments of activities performed in parallel, the Stages,
- separated by check points, the Gates
- where continuation is decided based on Criteria.

Exhibit 1: Stage-Gate Consists of a Set of Information-Gathering Stages Followed by Go/Kill Decision Gates



* Cooper, 2008, *The Stage-Gate: idea-to-launch process*

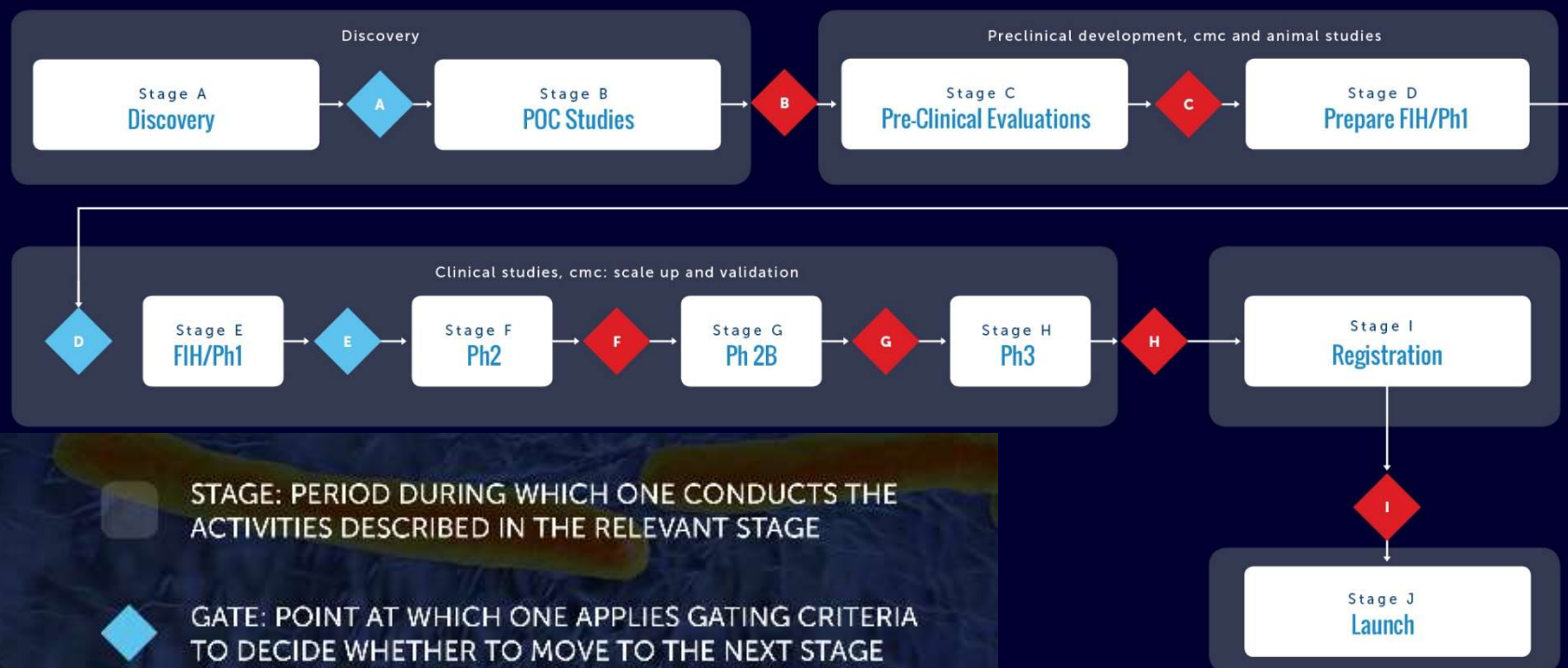
Structure of the Pathway

The Pathway is a matrix:

- Lines: Stages and Gates, from discovery to implementation
- Columns: expertise, as Functions
- Each box: activities, criteria, guidance with indications

TB VACCINE DEVELOPMENT PATHWAY

TBVacPathway.com



TBVacPathway.com

Introduction and Guidance

Stage Gates

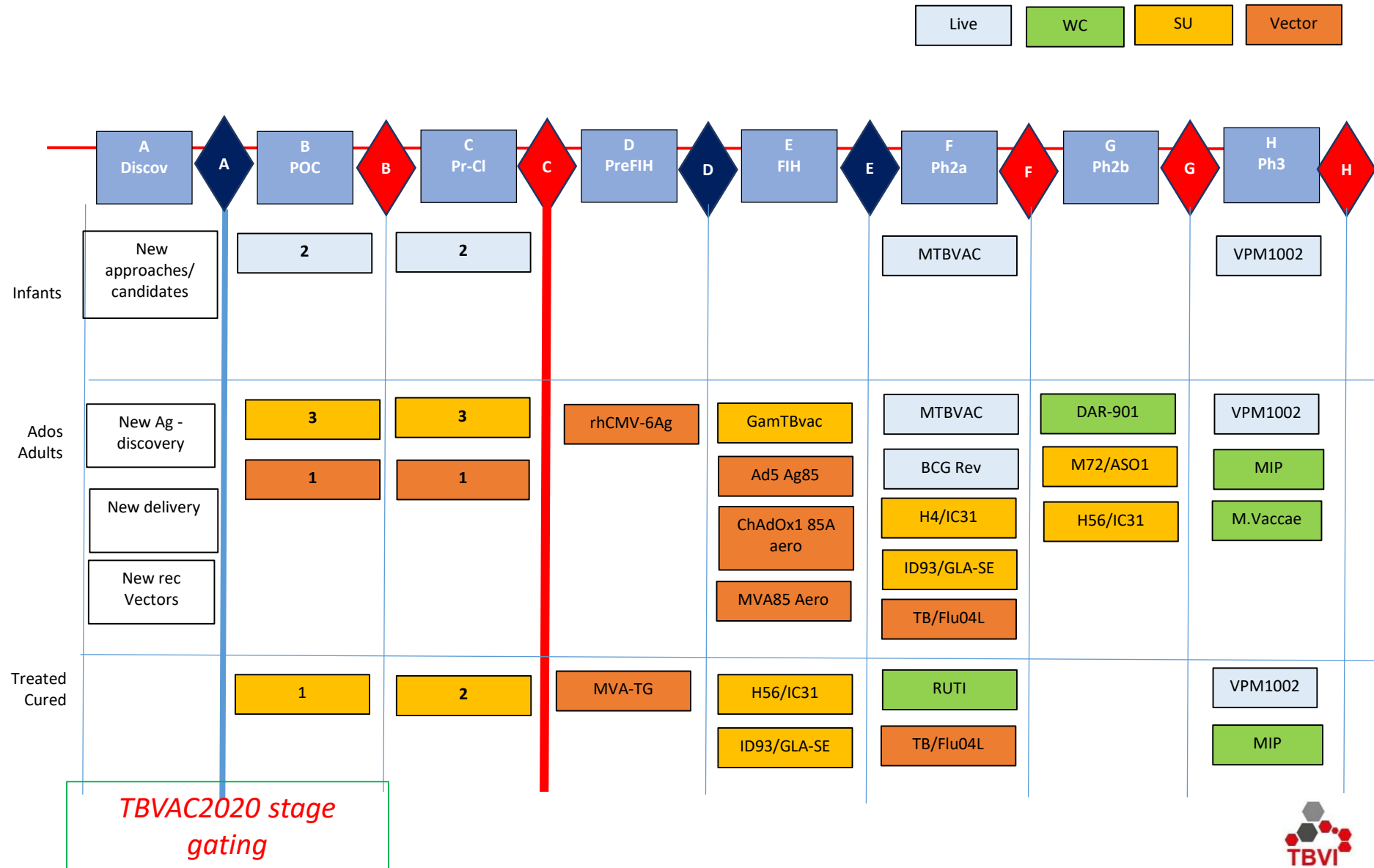
Functions

Feedback

Examples of use

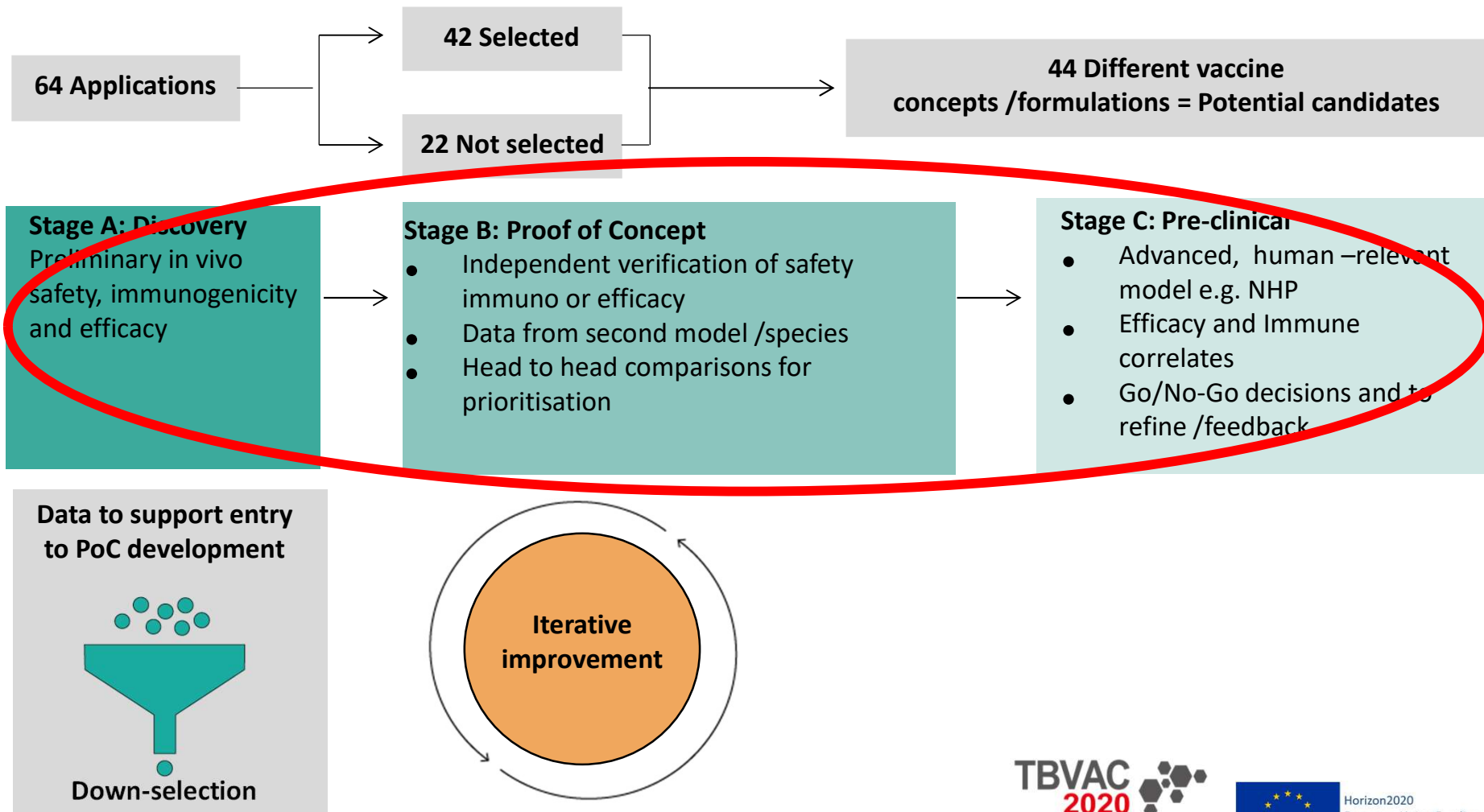
- Education: overview of development from concept to commercialization, progression of activities within each function
- By developers, as a guide for planning their research and development, monitor progress, refer to criteria for decision
- By organisations, to structure the portfolio of vaccine candidates per stages, indications and technologies and to document progression of candidates
- By committees, to use criteria for selection of projects

Example: structure of portfolio



Example : selection

Applications reviewed by Portfolio Management Committee
Selection based on stage-gate and prioritisation on criteria – up to Stage C



Moreover...

The Pathway ...

- Is generic and could be a baseline for the development of any vaccine, or a 'check list' of activities, deliverables
- Activities are sequential, no 'shortcuts'
- Refers to guidelines, publications, public information
- Continuously updated from feedback, surveys, with a revision in 2021

Conclusions

The Pathway is a body of knowledge and a data-driven methodology,

- that offers developers structure and guidance for their product development plan, from concept to commercialization,
- a structure to the TB vaccine pipeline, with objective criteria for assessment, selection and progression of candidates, critical for balanced investments and a healthy pipeline.

It is available on internet and free, with dissemination ongoing and a revision planned. Use it, share it, criticize it, contribute to it...

Acknowledgements

- BMGF
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Working Group



Georges Thiry, Leo van der Pool, Gerald Voss, Bernard Fritzell, Jelle Thole, Dereck Tait
Maria Lempicki, Anne Marie Graffin, Marit Holleman, Danielle Roordink, Ann Rawkins, Emmanuelle Gerdil
Missing on photo: Ann Ginsberg, Ilona van den Brink

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Thank you !

