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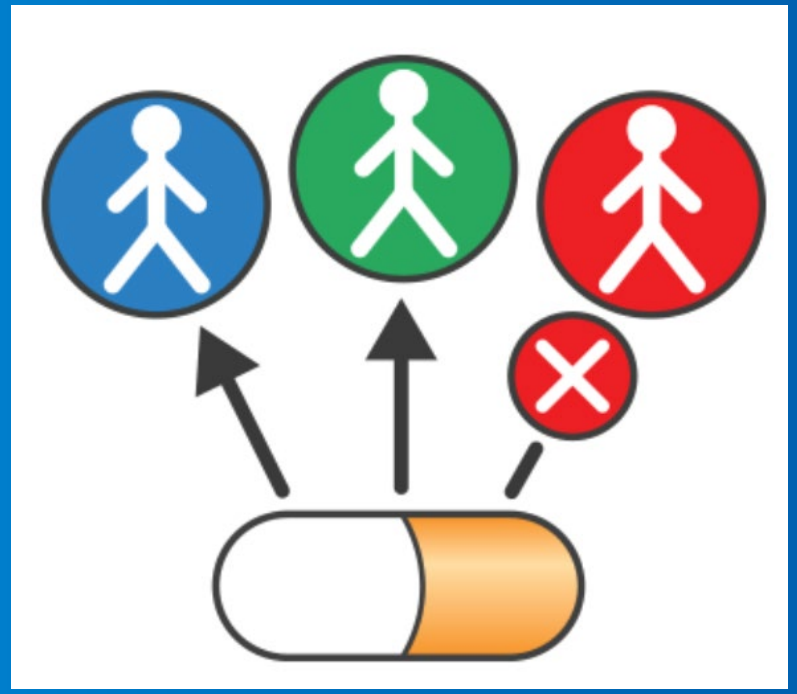

Companion Diagnostics: new role for medicine authorities?

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GOOD MEDICINES USED BETTER

In Vitro Diagnostics and Companion Diagnostics

Medicines regulation environment:

Biomarkers may be used to **select/stratify patients**

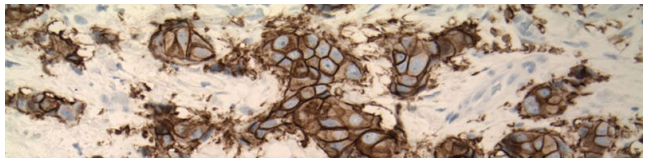
Subtype of In Vitro Diagnostics (IVD),
i.e., **Companion Diagnostic (CDx)**

Select patient expected to benefit or suffer from the drug

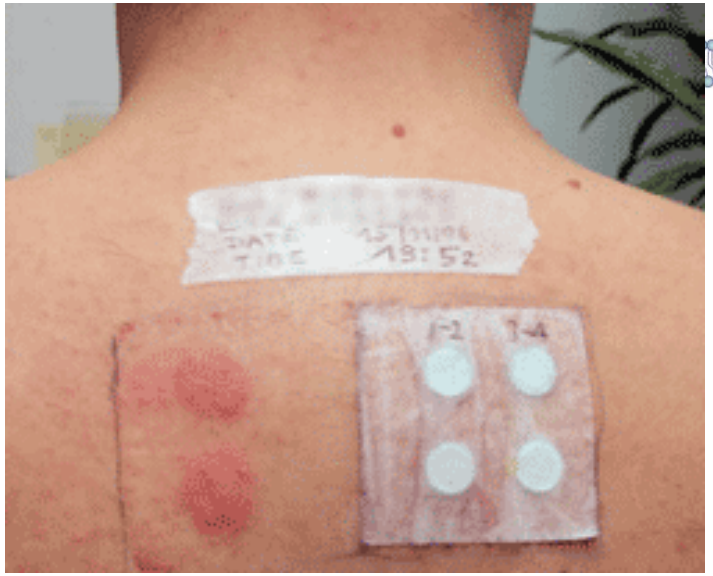
-Target receptor
-Immune system components (HLA components)

Typical examples of biomarker use/CDx

HER2 test for trastuzumab (Herceptin) in Metastatic or Early Breast Cancer.

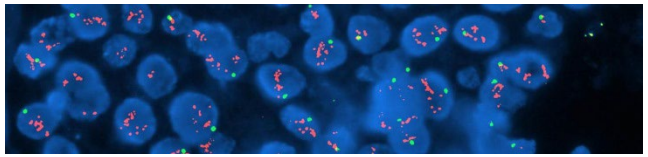


- Immunohistochemistry or in situ hybridization.
- Advice on the use of an IVD is indicated in the Summary of Product characteristics (SmPC)
- Many more in oncology: PD-L1, EGFR, KRAS, BRAF etc



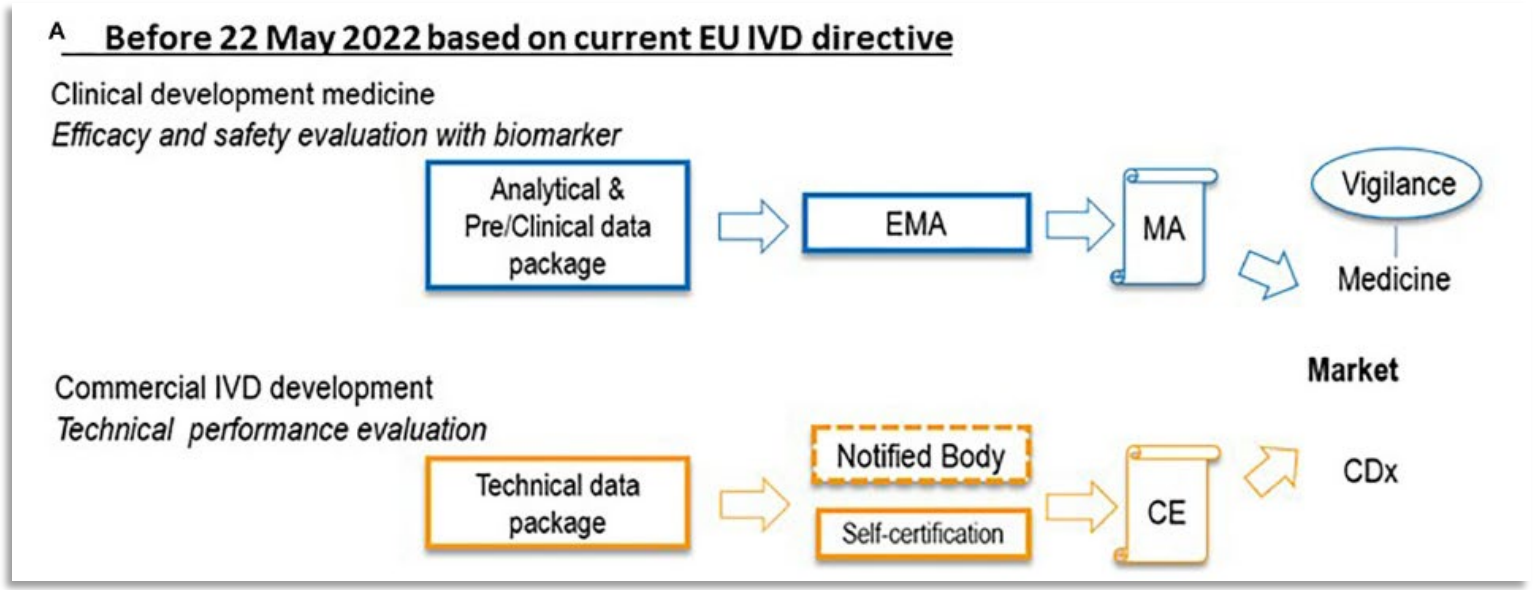
HLA-B*5701 test for abacavir (Ziagen), to exclude HIV patients with increased chance to develop hypersensitivity reactions

Use of an IVD/CDx is indicated in the **indication, posology** or **contra-indication** sections of the SmPC of the medicinal product

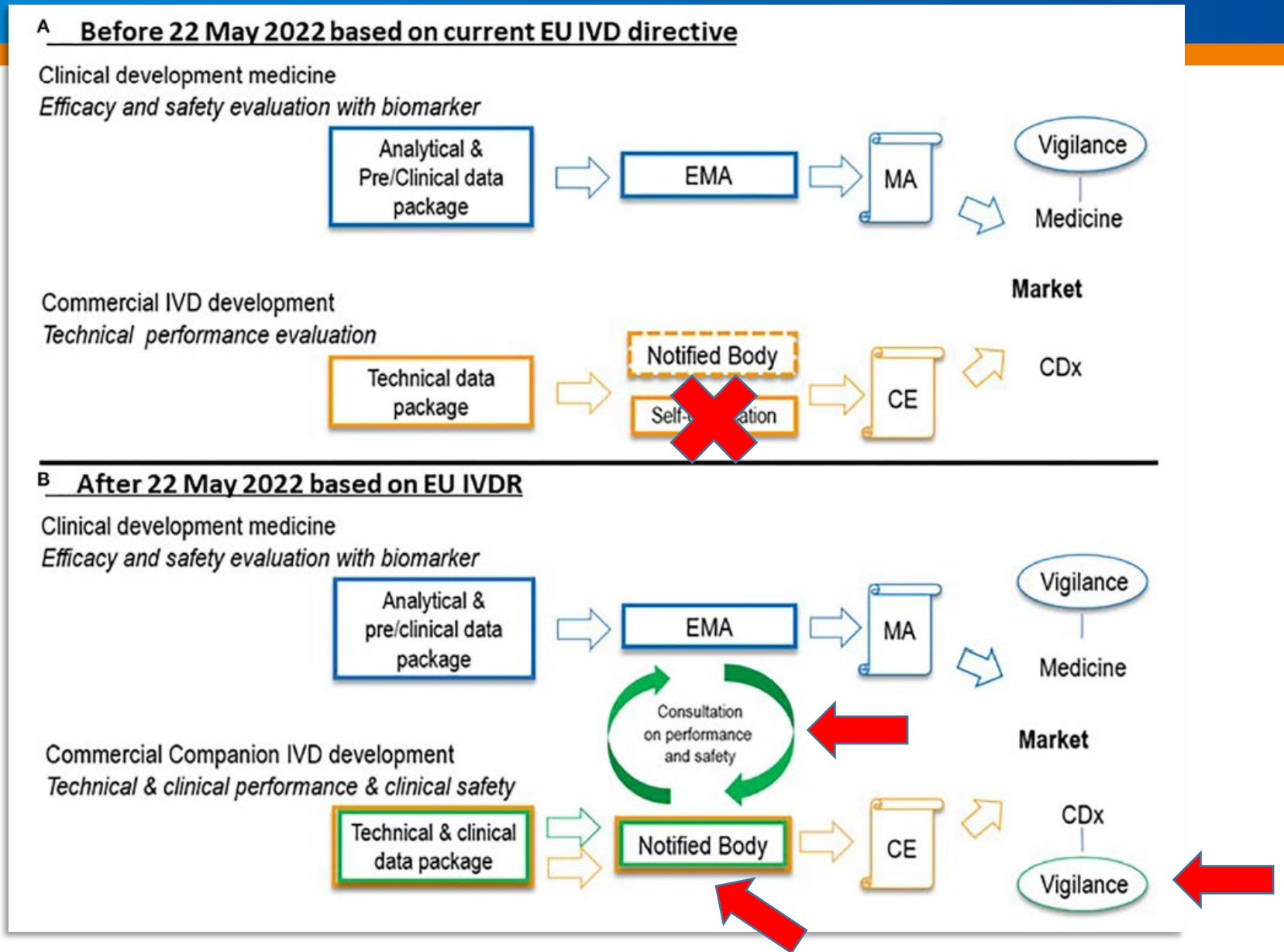


Previous regulation
IVD EU Directive 98/79/EC (IVDD)

- *In vitro diagnostics (IVD)* are regulated via the Notified Bodies
- IVDs may have or obtain a CE mark (**self certification**)
- IVD analytical and clinical package assessed by Drug Agency in relation to reliability of the clinical trial
- No general technical assessment IVD by Notified Body nor MEB/EMA



Previous IVD directive vs new IVDR



A CDx falls under the second highest risk classification (c) under the IVD regulation

- this reflects the risk to the patient should the test generate erroneous results.

CDx types and Timelines for new IVDR

Type of CDx in the IVDR:

1. New CDx, co-developed with a new medicine: CDx procedure runs in parallel
2. Already CE marked CDx (legacy biomarker assays)
3. Follow-on CDx (possible from May 2022)

IVDR implemented in May 2022 in stepwise fashion:

- New CDx and follow-on CDx should follow IVDR from **May 2022**
- Re-certification of legacy biomarker assay 'CDx' before **May 2026** (one year extension from initial date)

Is it all new for MEB/EMA?

Collaboration with NB on Companion Diagnostics: **yes**

Assessment Companion Diagnostics: ?

Timepoints:

Scientific Advice => prior to registration, during drug development => SA reports

Marketing Authorization Application => at time of registration => (public) assessment reports

Scientific advice procedures in 2016–2020
Registration in 2017–2019

Question: Information/questions raised on (potential) Companion Diagnostics?

Experience evaluation CDx by MEB/EMA

MAA

468 Marketing Authorization Applications in time period 2017-2019

301 generic/biosimilar excluded => 167

Screened SmPC on potential CDx => 20 (4%) (17/20 antineoplastic agents)

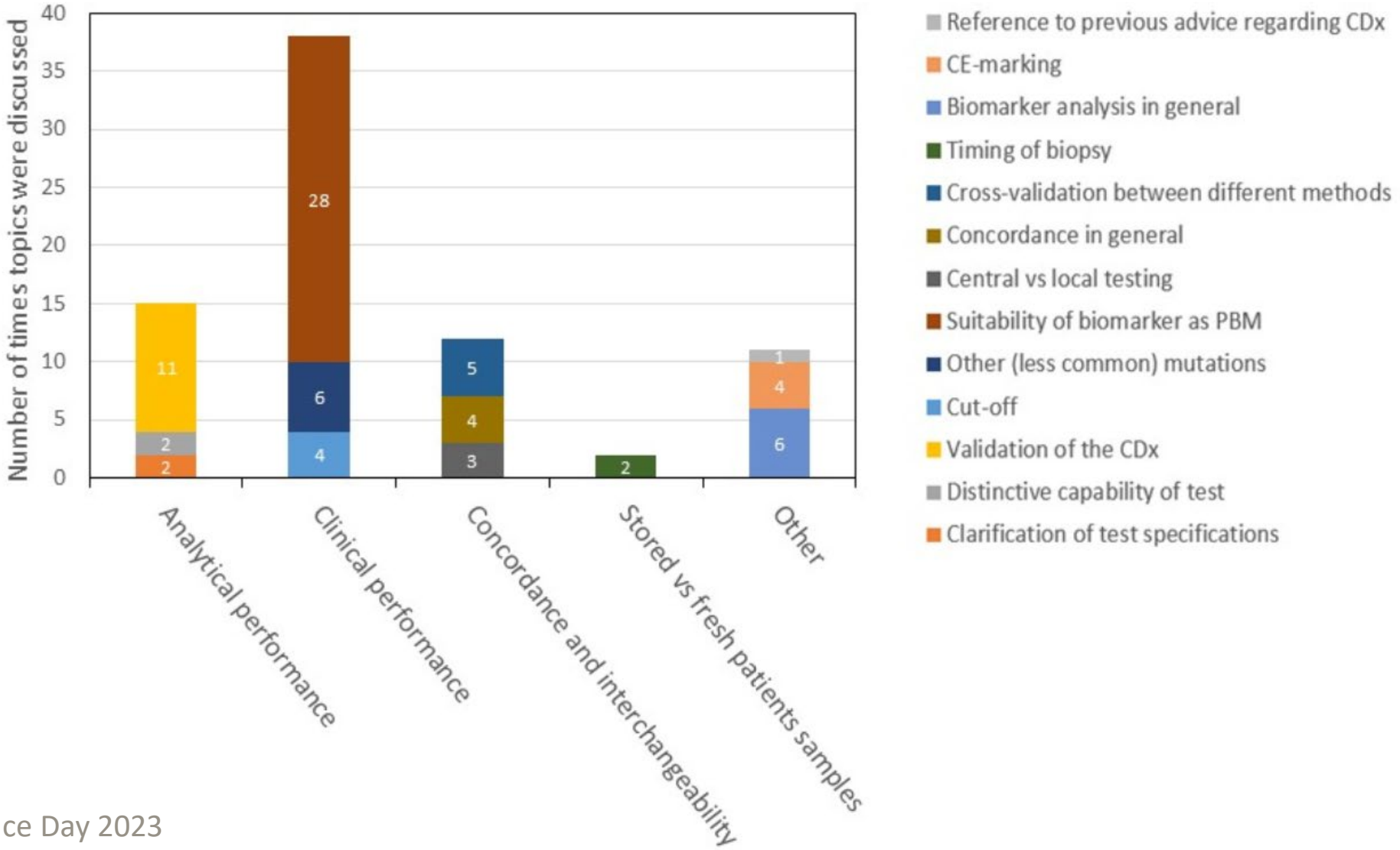
EPARs and internal ARs screened for CDx related remarks

SA

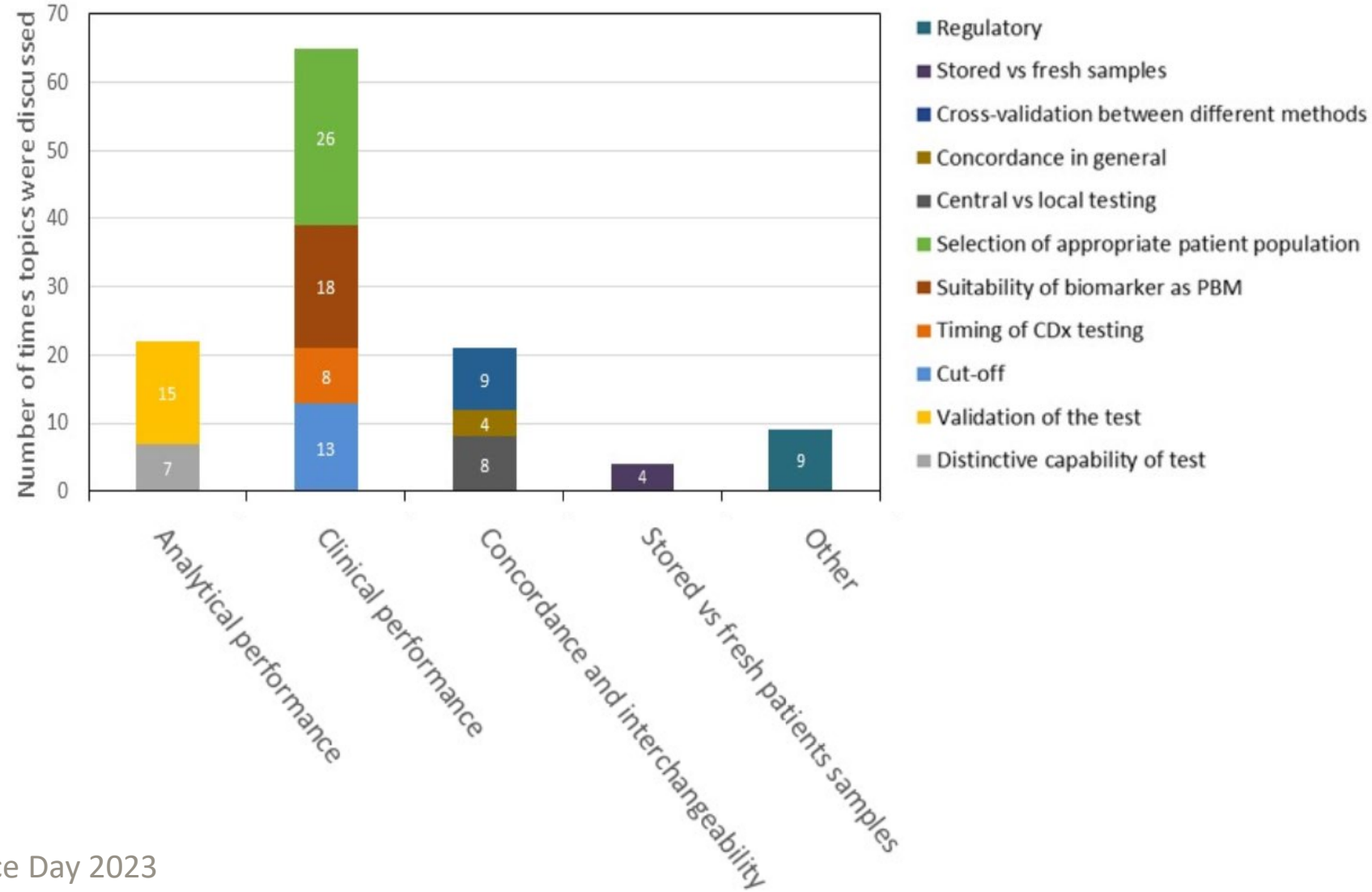
95 Scientific Advices in time period 2016-2020 (42/46 antineoplastic agents)

Screened for discussion on CDx in Question and Answer section=> 46 (48%)

Experience evaluation CDx by MEB/EMA: MAA



Experience evaluation CDx by MEB/EMA: SA



CDx experience MEB/EMA since May 2022

Consultation procedure from NB:

6 procedures, i.e., 5 legacy CDx, 1 follow-on CDx

CDx in dossier for a new medicinal product:

5 medicinal products with CDx involved

More formal assessment of CDx data contained in the dossier (preparation for the consultation procedure)

Experience evaluation CDx by MEB/EMA: Conclusions

- Joint assessment CDx important and an improvement as compared to the situation until 2022. This new procedure also poses a challenge to authorities.

- However, EMA and the individual EU member state drug agencies already have gained relevant experience with critically assessing the CDx as part of registration procedures for medicines.

- Gaining further experience with CDx consultation procedures, and MAAs for product with a CDx involved.

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