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AGENCY

Progress with the implementation of the Companion diagnostics framework under the EU In-vitro Diagnostic Regulation (IVDR)

Update on the final guidance

8th Industry Stakeholder Platform on R&D support

Monday 11 July 2022

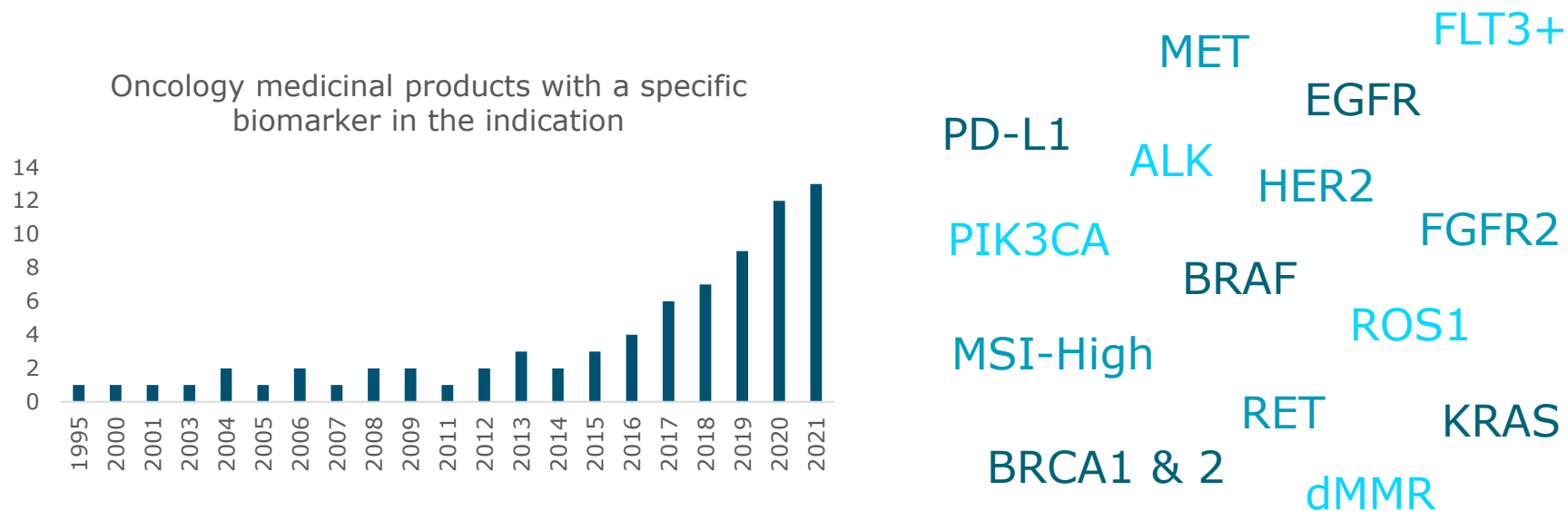
Presented by Ana Trullas and Ciska Verbaanderd
Office of Oncology and Haematology, European Medicines Agency

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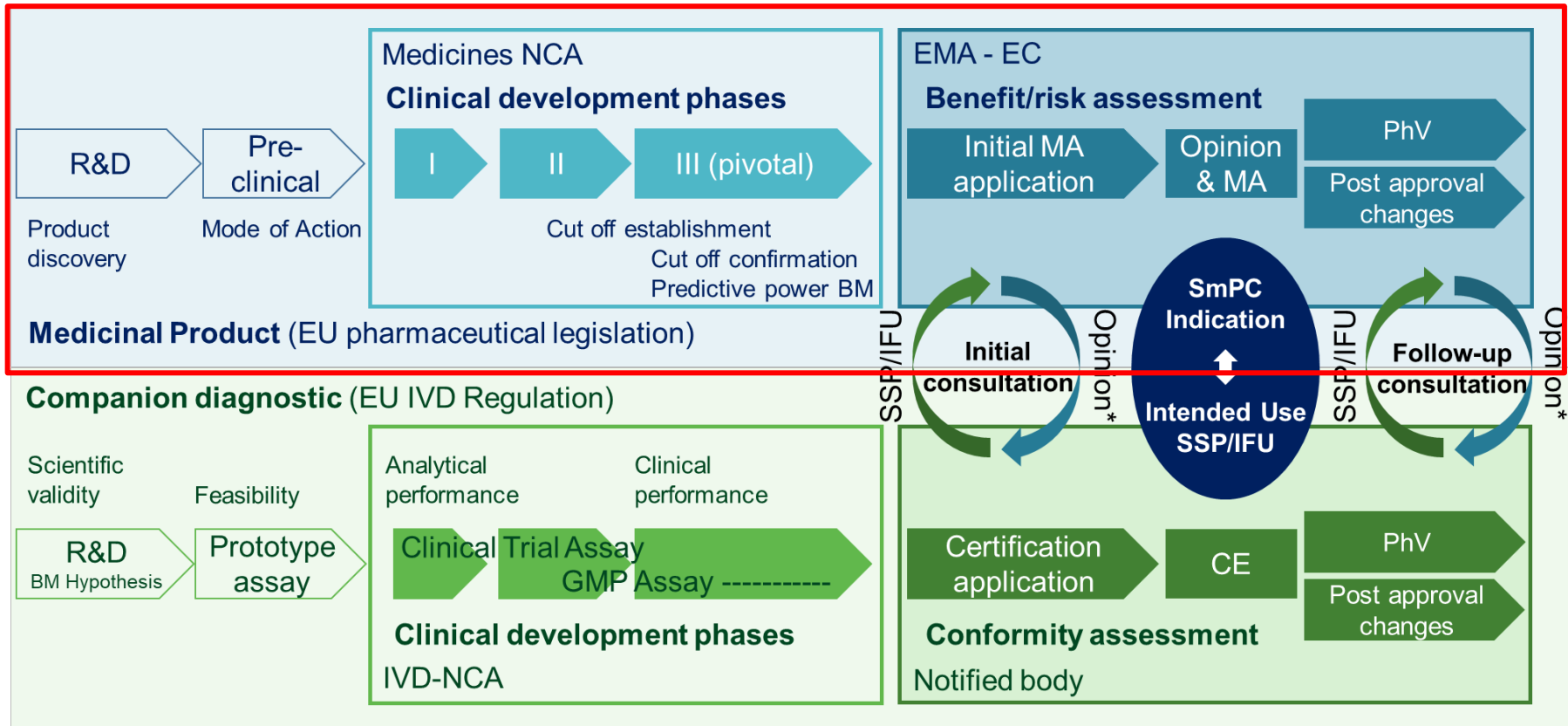


Why In-vitro diagnostics? Oncology examples

About 1/3 of marketing authorisations in the field of oncology, approved in EU between 2010 and 2020, required a diagnostic test for patient identification



Medicinal product & IVD/CDx interplay in Europe



Abbreviations: BM: Biomarker; CDx: Companion Diagnostics; EC: European Commission; EMA: European Medicines Agency; IVD: In vitro diagnostic medical device; MA: Marketing Authorisation, NCA: National Competent Authority; R&D: Research & Development

- ✓ Need for systematic review of predictive biomarker & assay (CDx) data
- ✓ Consideration to reflect information on the biomarker & assay in the SmPC

D80 AR template - In vitro biomarker test for patient selection for efficacy and safety

Scientific rationale for the choice of the predictive in vitro biomarker test (e.g. prevalence, relation to disease mechanism)

Analytical method including assay platform, specimen, pre-analytical processing requirements and read-out method.

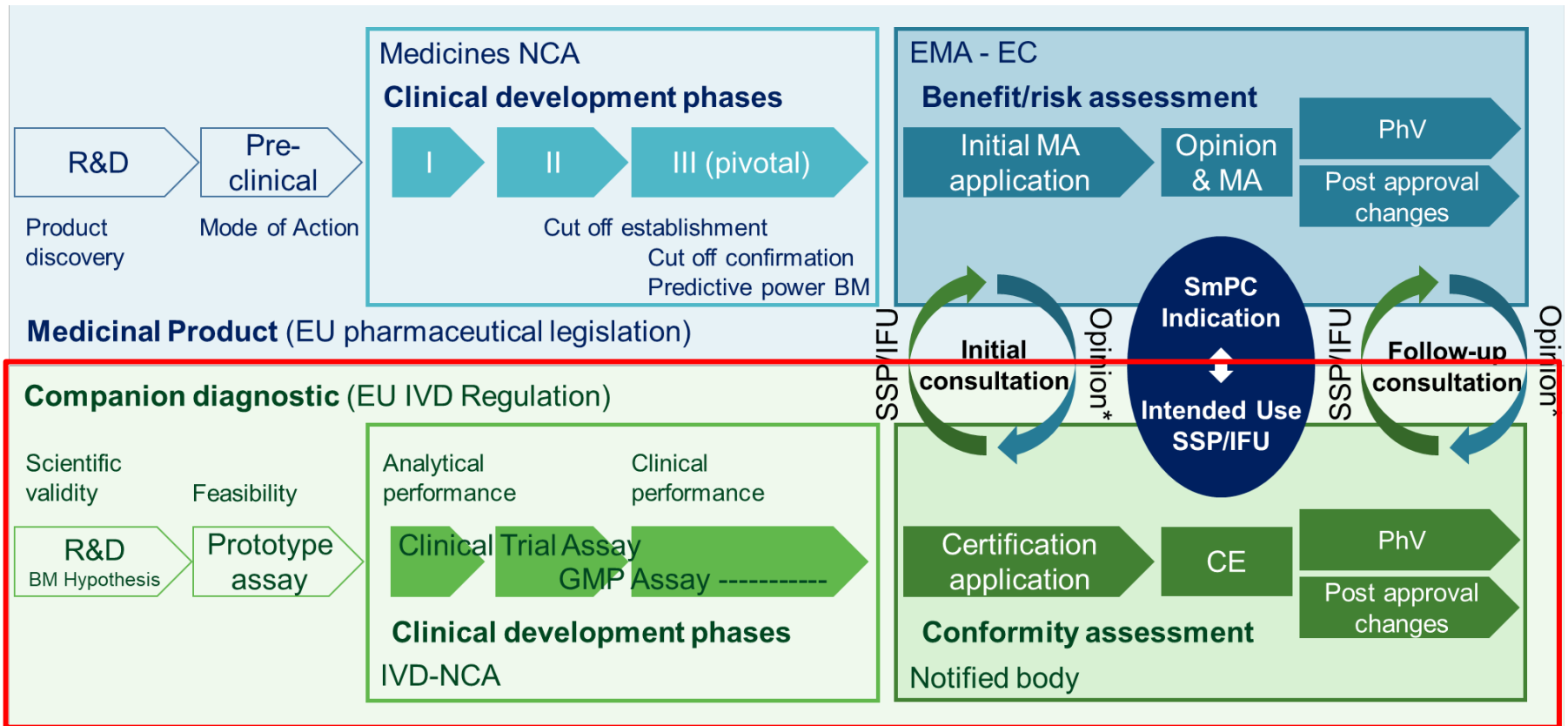
Consideration of the status of the assay in pivotal trial in relation to the intended CDx

Analytical and clinical validation strategy:

- *Analytical validity: For verifying the suitability of an assay, robustness, accuracy, specificity, sensitivity and linearity should be considered depending on the analytical platform*
- *Clinical validity (sensitivity/specificity) should be described either by correlation with a clinical endpoint (for novel assays) or -if available- by concordance study with a clinically valid reference assay*
- *Cut-point selection should be described and discussed in detail since it is of particular importance for the benefit /risk assessment*

[https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/assessment-templates-guidance#day-80-and-day-120-assessment-report-templates-\(containing-guidance\)-section](https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/assessment-templates-guidance#day-80-and-day-120-assessment-report-templates-(containing-guidance)-section)

Medicinal product & IVD/CDx interplay in Europe

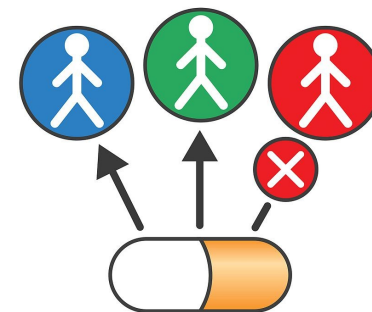


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CDx definition - Art. 2(7) IVDR

“ (7) ‘companion diagnostic’ means a device which is **essential for the safe and effective use** of corresponding medicinal product to:

- (a) **Identify**, before and/or during treatment, **patients** who are most likely to **benefit from the corresponding medicinal product**, or
- (b) **identify**, before and/or during treatment, **patients** likely to **be at increased risk of serious adverse reactions** as a result of treatment with the corresponding medicinal product. ”



Conformity assessment - IVDR Article 48

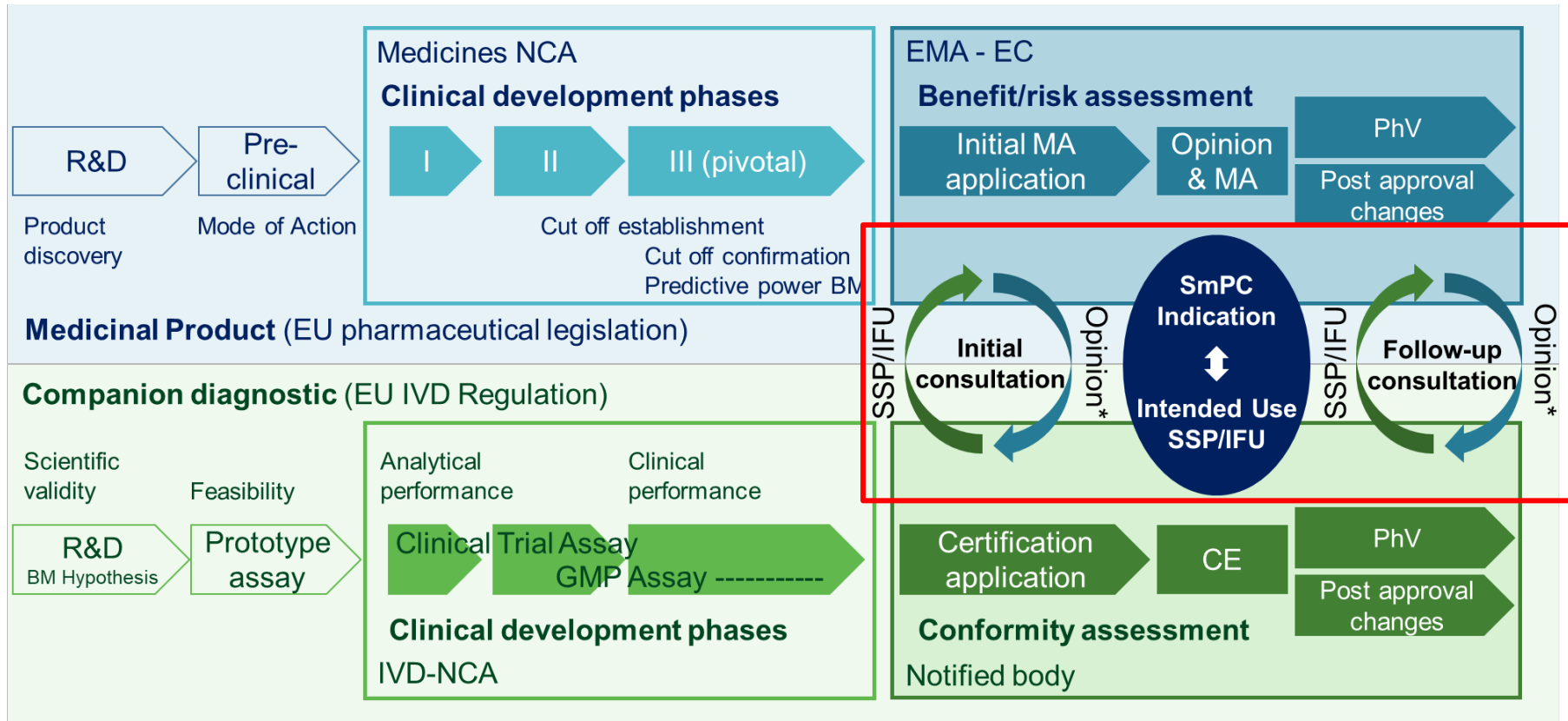
For **companion diagnostics** the **notified body** shall consult the concerned **competent authority** designated in accordance with Directive 2001/83/EC or the European Medicines Agency (**EMA**), as applicable



SSP & IFU - ANNEX IX, Chapter II - 5.2

The **notified body** shall, before issuing an **EU technical documentation assessment certificate** for the companion diagnostic and on the basis of the **draft summary of safety and performance** and the **draft instructions for use** [...] consult one of the competent authorities [...] **regarding the suitability of the device in relation to the medicinal product concerned.**

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Scope of assessment: Suitability of the CDx for use with the concerned medicinal product(s)

“**Suitability**” relates to the use of a CDx with a particular medicinal product(s), given the performance and use claimed by the manufacturer.

Aspects that are considered when assessing the suitability of a CDx:

- Scientific validity (scientific rationale)
- Analytical performance
- Clinical performance

- **Co-developed CDx:** a device that is developed in a clinical development program together with the concerned medicinal product, either in view of an initial marketing authorisation or a change of the indication. This can mean that the device was developed in the framework of:
 - A pivotal clinical trial with the concerned medicinal product
 - A bridging study assessing the concordance of the CDx and the device used in the pivotal clinical trial of the corresponding medicinal product
- **Follow-on CDx:** a device that seeks the same indication in its intended use as the co-developed CDx (hereafter, original CDx). The follow-on CDx targets the same biomarker but is not developed in parallel with the clinical development programme of the medicinal product and is not necessarily based on the same technology as the original CDx.
- **Devices already marketed under Directive 98/79/EC on in vitro diagnostic medical devices (IVDD).** The two scenarios above are possible depending on how the device was initially developed. → For Class C devices, transitional period for application of IVDR requirements until 26 May 2026

Overview of steps for implementation of CDx consultation

Dec 2022

Publication of draft guidance and procedural documents

Jan 2022

First CDx consultation submitted to the EMA

Feb 2022

End of public consultation on the procedural guidance

Jun 2022

Adoption of guidance and procedural documents by CHMP/CAT

- **Guidance on the procedural aspects** for the consultation to the EMA by a notified body on CDx
- **Assessment Report template** for consultation on CDx
- **Application forms** for initial and follow-up consultation on CDx
- **Letter of intent-template** for the submission of a consultation
- **Q&A** on practical arrangements on the CDx consultation procedure

Guidance on the procedural aspects for the consultation to the European Medicines Agency by a notified body on companion diagnostics

Adoption by CAT for release for consultation	10 December 2021
Adoption by CHMP for release for consultation	16 December 2021
End of consultation (deadline for comments)	20 February 2022
Adoption by CHMP	13 June 2022
Adoption by CAT	17 June 2022
Date for coming into effect	Publication date

Keywords	<i>Consultation, notified body, companion diagnostic, in vitro diagnostic, medical device, biomarker</i>
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[Medical devices | European Medicines Agency \(europa.eu\)](#)

Initial consultations (60-day TT with a possible extension of 60 days)

- Pre-submission phase
- Submission & validation
- Assessment (ad hoc CHMP/CAT discussion)
- Adoption of Opinion or List of Questions (LoQ)

Follow-up consultations (30-day TT, no extension)

[Procedural timetables | European Medicines Agency \(europa.eu\)](#)

- **Publication of the CHMP assessment report** on the CDx consultation
 - Reflection of information on **CDx in the SmPC** of the medicinal product
 - Clarification of **scope of NB and CHMP/CAT assessments**
 - Opportunities to get more accurate **estimates for expected CDx consultations**
- Learning curve for all stakeholders involved
- Need for further close interactions between stakeholders, including medical device and pharmaceutical industry, to facilitate and optimize this process

Thank you for your attention

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Further information

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