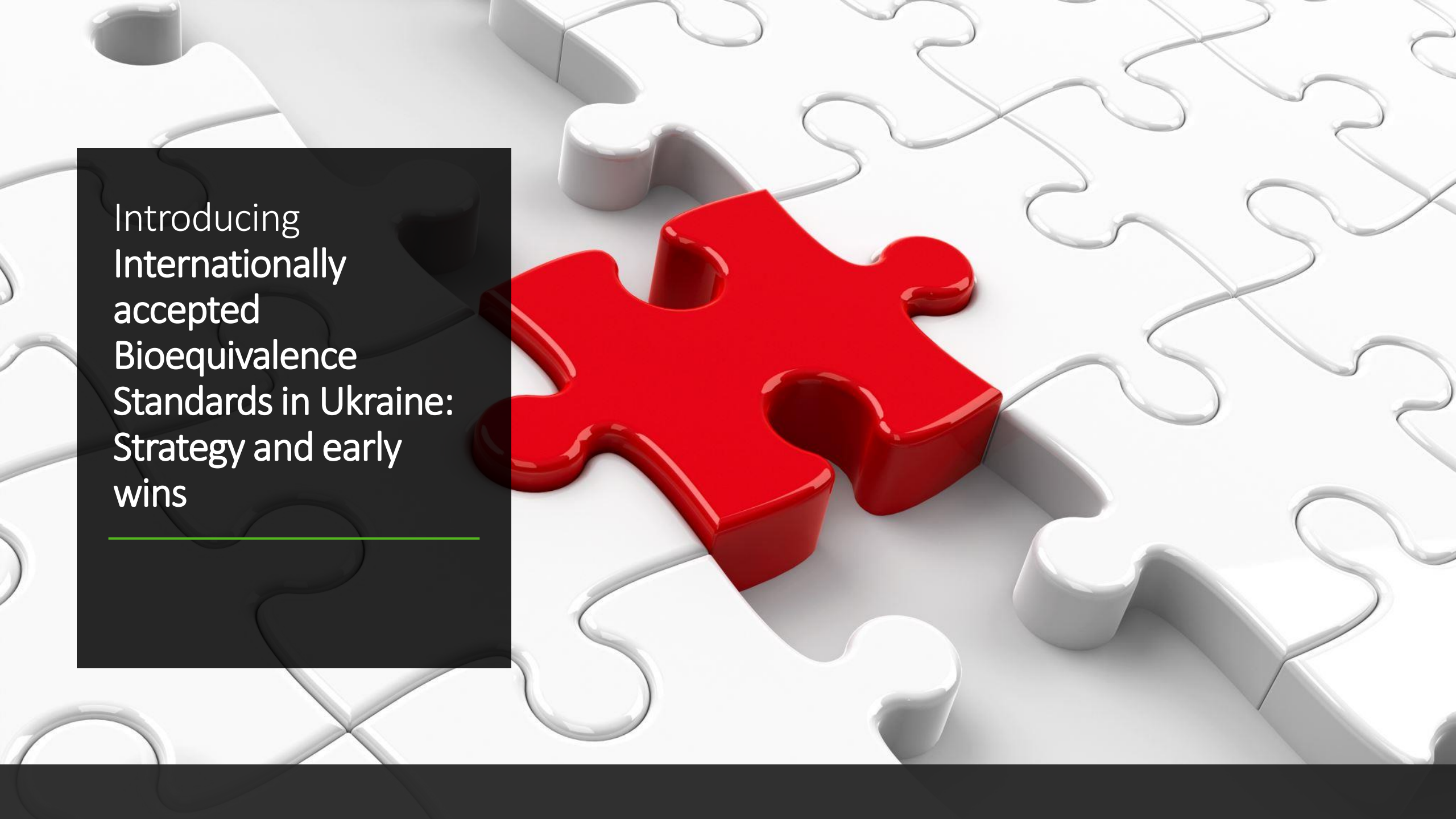

Introducing Internationally accepted Bioequivalence Standards in Ukraine: Strategy and early wins

- **To promote the use of generics** is an important tool to cap national healthcare spending on medicines.

  In general they cost only **about 20%** of the originator's price. Cost savings due to generics are tremendous: in the USA in 2018 cost savings of about 293 billion USD were achieved

- Generic products (including hybrids and biosimilars) represent **the by far biggest share** in all pharma markets: in general about 80% by volume, but only about 30% by value

- Consequently, it is therefore of paramount interest that generics, branded generics and hybrid medicinal products on the market are **safe, efficacious and of good quality**

- Generic drugs must fulfil **the same requirements** concerning quality, safety, and efficacy as the originator drug, i.e. both drugs must be **pharmaceutically equivalent**. In order to provide evidence that the test medicinal product is as safe and efficacious as the reference drug its **bioequivalence has to be demonstrated.**

- Drugs that confirmed their bioequivalence to the reference product are considered as **therapeutically equivalent**.

- Therapeutic equivalency is the basis for the ultimate goal of a generic medicine i.e. to be **interchangeable** with the reference product.
  Interchangeability includes not only equivalence of the dosage forms, but also of the indications and instructions for use.

- **Biosimilars** cannot be bioequivalent, as they are produced by biotechnical processes and the originator's cell line cannot not be identical to the one of the originators.

Goal: to develop the bioequivalence strategy for Ukraine

Methodology:

- Literature review of respective laws, decrees, regulations, rules and guidelines covering regulatory/legislative framework in both Ukraine and EU;
- Identification of possible differences, discrepancies and non-conformities;
- Draft conclusions and recommendations to outline long-term implementation strategy;
- Discussion with key stakeholders -- SEC, pharmaceutical industry represented by business associations, two clinical research organizations performing bioequivalence studies in Ukraine, and the WHO.

Introducing New Strategy on Bioequivalence in Ukraine
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The in-depth analysis showed that relevant provisions in EU and Ukrainian systems are similar, but still need harmonization.

Key challenges:

- Differences, non-conformities and discrepancies in the Terms and Definitions within the Ukrainian legislative/regulatory system and between the Ukrainian and EU/EEA
- Differences, non-conformities and discrepancies in the general legislative/regulatory frameworks
- Differences, non-conformities and discrepancies in the regulations on the investigation of bioequivalence of generic drugs/hybrids

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However, important differences existed not only between Ukrainian, EU/EEA, WHO, and FDA rules, but also **within** the Ukrainian regulatory system itself.

The identified differences in the regulatory systems are directly related to the evaluation of bioequivalence and **its role** in many areas and processes, **like marketing authorization, procurement, reimbursement, price regulation, drug safety and efficacy.**

International experience of generics interchangeability (examples from EU)

1. Sweden (MPA)

- There is a list of "Substutionable medicinal products" on MPA's homepage, which is frequently updated and revised. Basic principle for substitution is that "the products have the same active substance in the same amount and are otherwise **medically equivalent**" (a unique definition!)

2. Ireland (HPRA)

- Definition of an interchangeable medicines and criteria for them;
- 9 conditions, which apply to the list of interchangeable medicines;
- HPRA has a process for developing the list of interchangeable medicines

International experience of generics interchangeability (examples from EU)

3. Germany

- **Guideline on generic substitution** (Good substitution practice) for pharmacists
- Physician decides on generic substitution by ticking (or not) a box on the receipt *"aut-simile"*
- List of medicines forbidden to be substituted exists as well as a **negative list** for not-reimbursed products
- Co-payment between 5 and 10 € for each prescription
- Doctors have a budget per patient. If the doctor exceeds the limit, he might be personally liable for re-payment

International experience of generics interchangeability (examples from EU)

3. Germany

- 2 types of substitution: first-time administration and changing the medicine during an ongoing therapy
- Reference prices for reference groups (defined products in a therapeutic class)
- No imbursement for OTCs, treatments for minor ailments, life-style medicines

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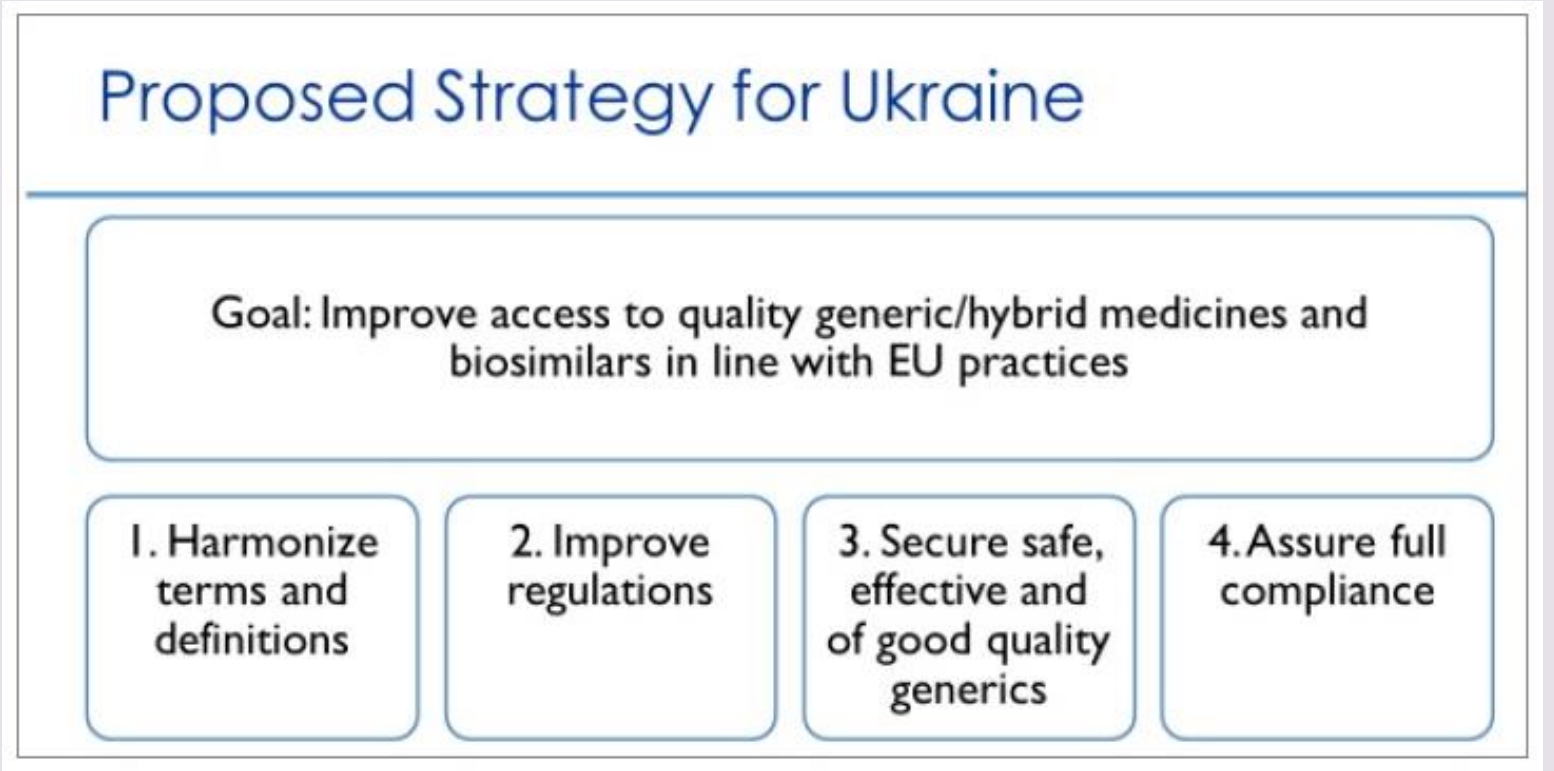

Some recommendations

- Create a list of **reference** medicines
- Create a list of **interchangeable** medicines
- **Classify** all registered medicinal products in Ukraine by their equivalence into categories, for example:
  - studies are not required;
  - studies were not conducted;
  - bioequivalence with the reference drug was proved.
- Set up **quality criteria** for allocation of budgetary funds to provide population with medicines via reimbursement or procurements

Status Quo

- On November 2, 2018 a new version of the MOH **Guideline** 42-7.2:2018 “Medicines. Bioequivalence research” was adopted

- The following steps have been taken to make the quality, safety and efficacy of medicines **available to the public**:
  - On September 4, 2018 the Parliament approved the Law No. 2519-VIII “On Amendments to Art. 9 of the Law “On medicines” concerning access to results of preclinical study and clinical trials”;
  - On June 27, 2019 the MOH Order was approved, requiring applicants to submit pre-clinical and clinical trial reports when registering drugs. Such reports should now be published on the official website of MOH.

- On February 5, 2019 a **Working Group** on bioequivalence of medicines was created to bring together all major stakeholders.