Healthcare System Reform & Innovative Medicine in China

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RDPAC
2016 APAC, April 7th, 2016

Content

Healthcare reform and market trend

- Progress and Key issues
- Major Reform policies for pricing, reimbursement and bidding
- Pharma market trend

Regulatory reform for innovative medicines

- Document No. 44 by the state council
- Impact of Self inspection and audit of clinical trial data
- New Category for chemical drug registration
- Prioritized review for new drugs
- Ecosystem for drug innovation

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China's healthcare and pharmaceutical reform since 2009 implemented different pilots and tools

After multiple round mandatory price cuts in the past, hospital purchase price is believed to be the key cost control factor.

Old healthcare reform 2005 — 2009 **Start of new healthcare reform** — 2015

Before 2009, new drug approval, GMP, public hospital management policies were adjusted almost annually

Pilots were encouraged at regional level to explore better healthcare mechanism:

- 1993, hospital bidding
- 1998, urban employee reimbursement system (UEBMI)
- 2003, NRCMI
- …

Drug reform

- **2009** EDS establishment, NEDL 2009
- **2010** cGMP
- **2013** NEDL 2012, Generic Consistency Evaluation
- **2015** **Free drug pricing**, accelerated drug approval, biosimilar guidelines, generic guidelines, cGMP deadline
- Multiple round drug price cut by NDRC

Medical service reform

- **2009** Public hospital bidding
- **2013** County public hospital reform
- **2015** City public hospital reform
- Separation of Rx and dispensing (e.g. zero mark-up)
- Tiered diagnosis and treatment
- Multiple round tenders

Reimburse-ment

- **2009** More financial support, 90% coverage, OOP burden: 55%
- **2014** 99% coverage, OOP burden: 33%
- **2015** **Reimbursement payment standard**, Critical Illness Insurance
- Coverage increases, OOP burden lowered

Planned Reimbursement standard is supposed to control drug prices by reimbursement similar to German FRP system

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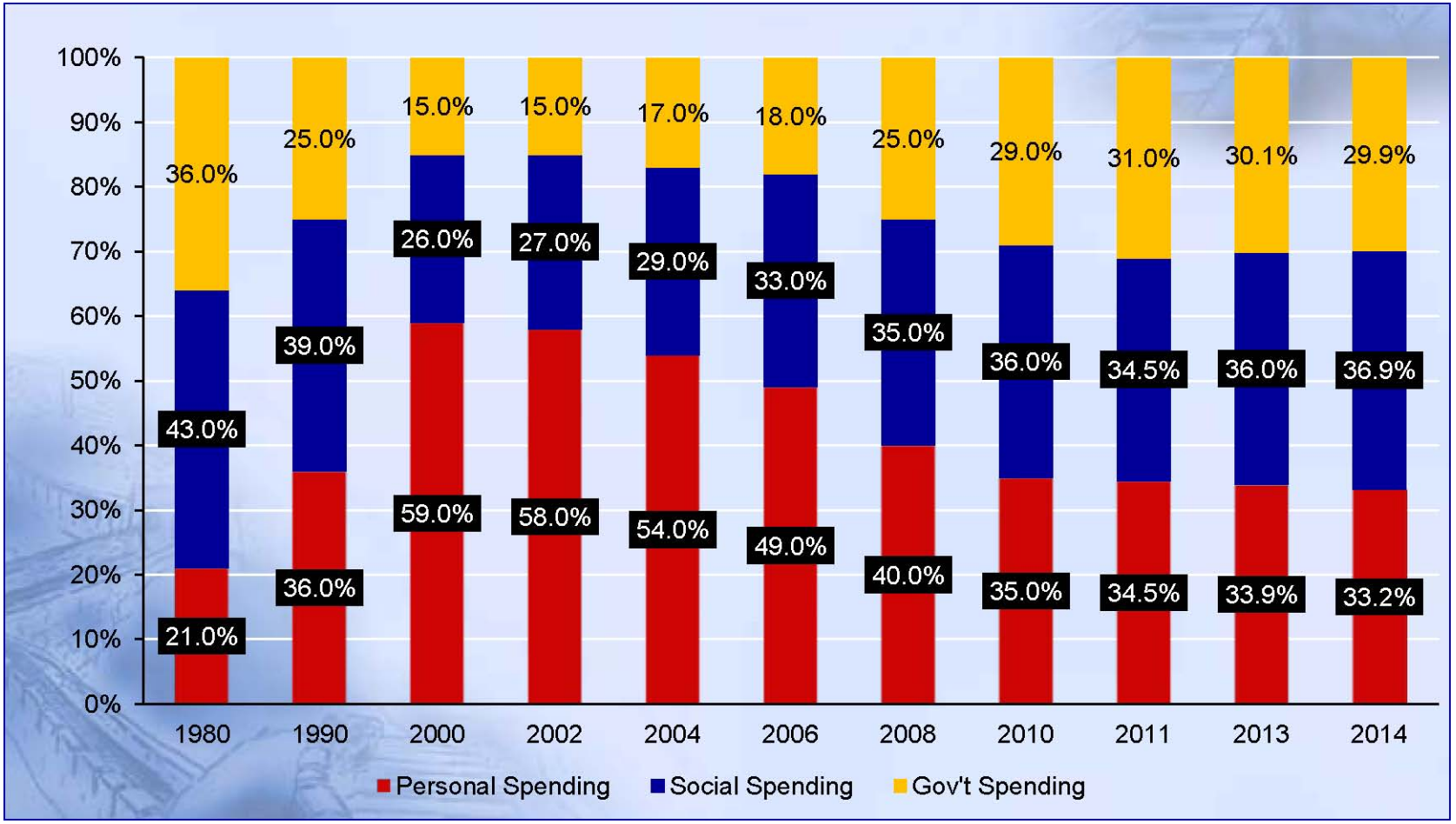
Healthcare Reform

Healthcare Spending by Funding Source (CNY bln)



Source: MOH / NHFPC

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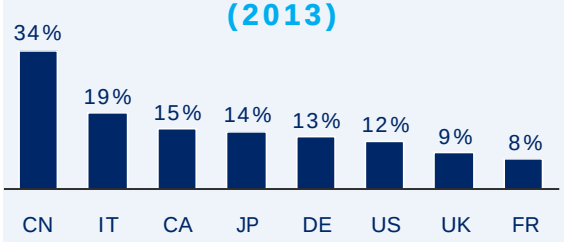
Despite progress, significant hurdles remain that challenge the sustainability of the Chinese healthcare system

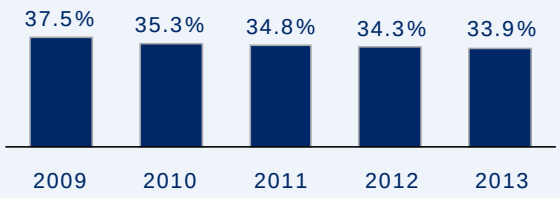
Key Challenges of China Healthcare System

High Patient Out-of-pocket Costs

Patient OOP as % of Healthcare Expenditure in Global Markets (2013)



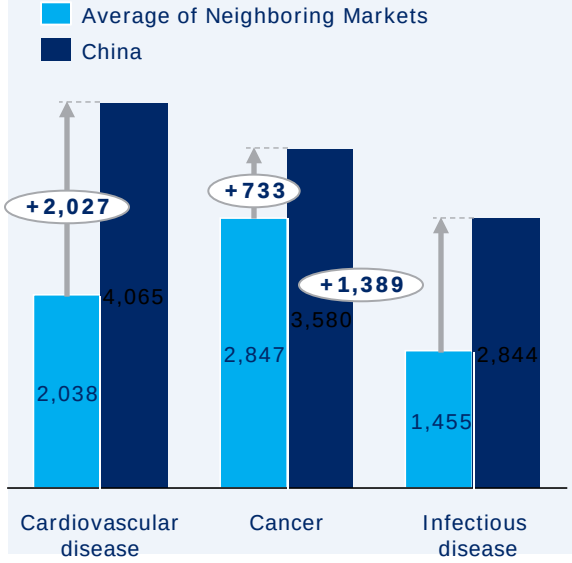
Patient OOP as % of Healthcare Expenditure in China (2009-2013)



Alleviate patient financial burden

Growing Diverse Clinical Unmet Needs

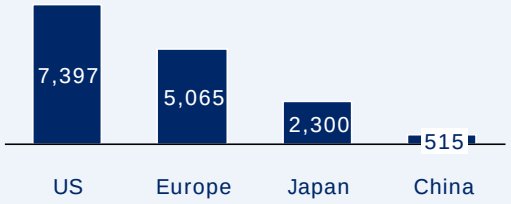
Disease Burden in China vs. Global Markets
(Age-standardized DALYs per 10^5, 2010)



Improve healthcare quality and efficiency

Far Behind in Fostering Innovation

Biopharma R&D Investment in 2012 (Bn RMB)



Median time for new active substances approved in emerging markets
(2007-2011, calendar days)

Promote the development of health industry

Source : WHO Global Health Expenditure Database, 2013;China Statistical Yearbook 2000-2012 , National Data from National Bureau of Statistics of China 2000-2012, IMS analysis; New England Journal of Medicine;

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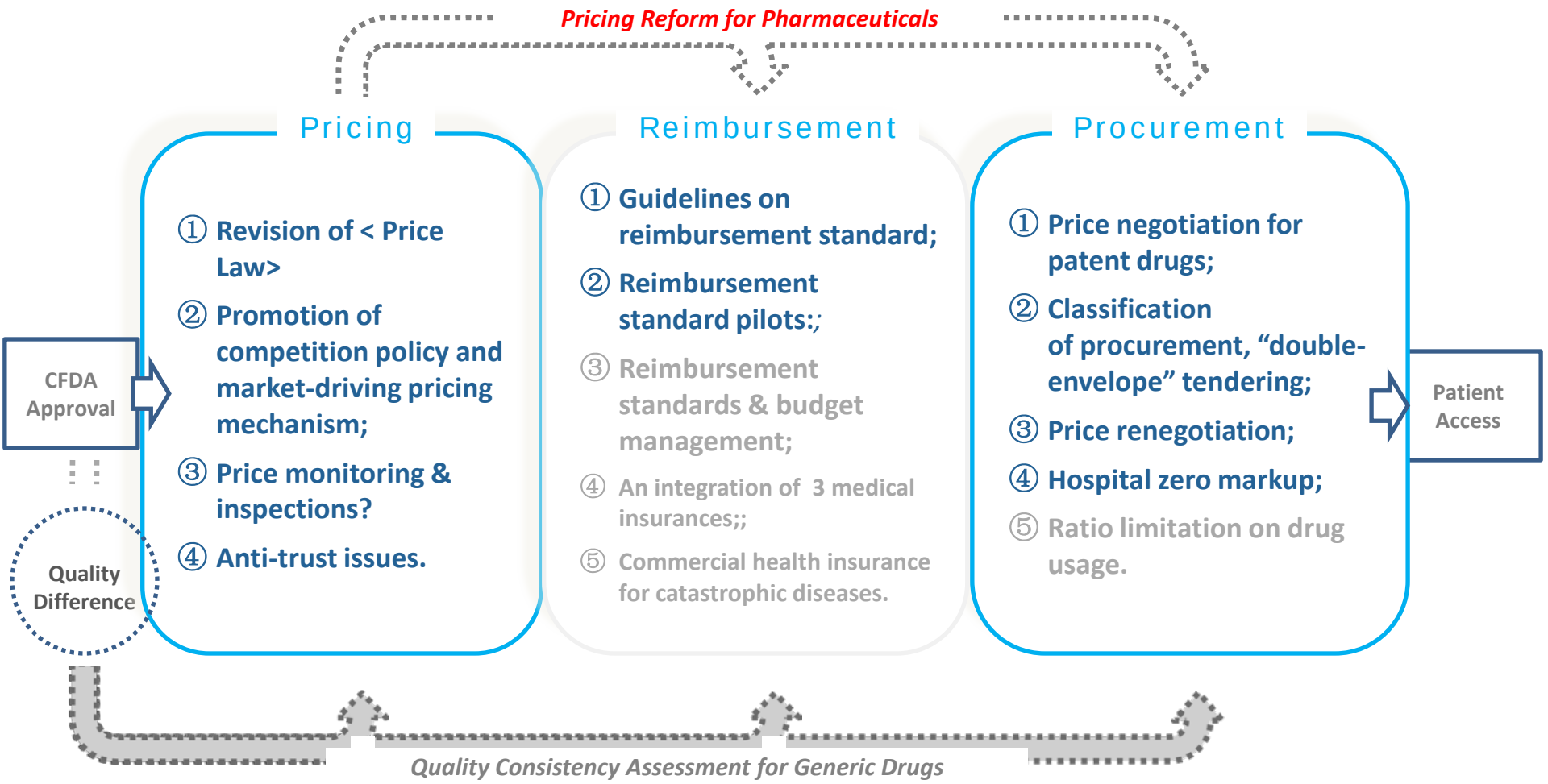
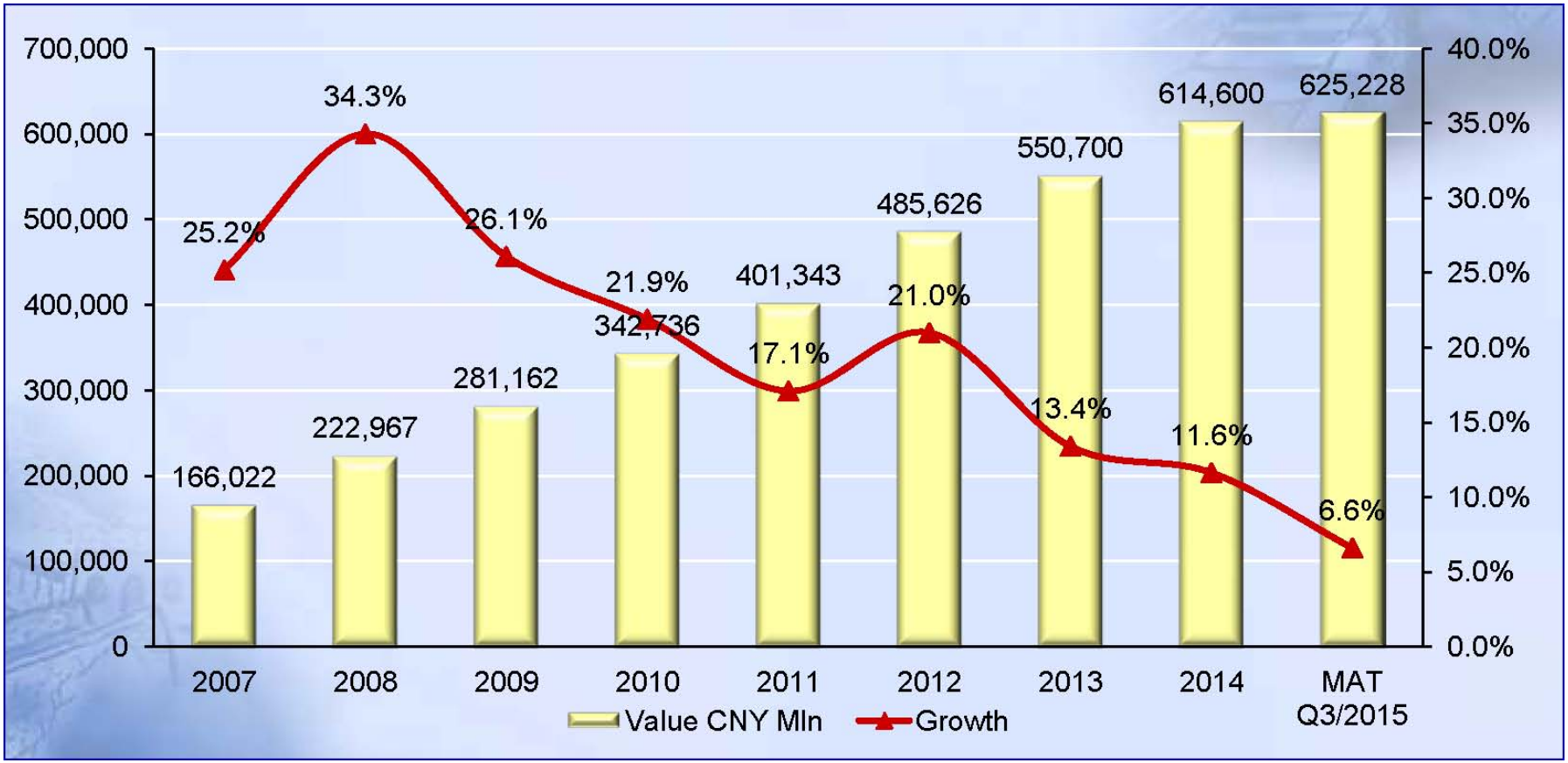
China Healthcare reform: Major policy changes for pricing, reimbursement and drug procurement in 2015



The Chinese Pharmaceutical Market trend

Chinese Hospital Market Growth 2007-2015



Source: IMS *Note: Hospital market with over 100 beds*

- MAT growth for Q3 of 2015 dropped to 4.9%. IMS projects 9% CAGR for Chinese hospital market 2015-2019
- IMS projects the market share of county level hospitals to rise from 26% in MAT 10/2015 to 40% in 2020. Market shares of MNCs and domestics on county level market are 86% and 14% in MAT 10/2015. Such sales account for 29% and 15% of domestic and MNC hospital drug sales.

Highlights of Regulatory changes since 2015

Reform signal

- **May 27. 2015** — New Registration Fee Standards for Drugs and Medical Devices
- **Jun, 2015** — Publication of 2015 China Pharmacopeia
- **Jul 22, 2015** — CFDA announcement on Clinical Trial self-inspection and verification
- **Aug 18, 2015** — **The State Council opinions on drug review and approval system reforming (Doc. No. 44)**
- **Nov 11 , 2015** — CFDA certain policies for drug registration review and approval (No.230)
- **Dec 01, 2015** — CFDA announcement on chemical drugs BE filing
- **Feb 25 2016 & Beyond** —
  - CFDA opinions on priority review and approval to resolve the backlog of registration **(Doc. No. 19)**
  - CFDA announce of chemical drug registration category reform **(Doc. No. 51)**
  - Upcoming DAL and DRR revision

Directional & Positive

1.Resolve backlog

2.Improve drug quality

3.Encourage innovation

4.Optimized/ streamlined regulatory procedures

5.Pilot MAH

Still Remained Challenges:

✓New Drug Definition and Chemical Drugs registration Classification

✓Lack of tangible implementing and systematical coordination

✓Need CFDA clarity the key uncertain areas

RDPAC Assessment on No. 44 Document

Opinions of the State Council on Reforming the Review and Approval System for Drugs and Medical Devices (State Council Document 2015 No.44) on Aug 18

In General

This document is the directional guidance for CFDA Regulatory reform. Given the high profile announcement from the State Council, the CFDA is mandated to implement and ensure success of the reform. It is very positive for China Bio-pharma Industry development in overall. The implementation regulations need to be in place subsequently

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Key Positive Areas

1. **Resolve the backlog** of registration applications, try to clear the backlog inventory before the end of 2016 and achieve the timeline required in the upcoming DRR revision by 2018

2. **Improve the quality of generic drugs**. Evaluation and approval of generics will be based on reference listed drugs(originators) as reference preparations to ensure consistent quality and efficacy of newly approved generic drugs in comparison with reference list drugs. By end of 2018, try to complete the quality consistent evaluation between oral preparations and reference preparations of national essential drugs

3. **Encourage Biopharm innovation** oriented towards clinical value and accelerate the evaluation and approval of innovative drugs (the scope is listed), encourage China to have **Global Simultaneous Development** for new drug development and participate MRCT including the early development (Phase I&II). MRCT data can support NDA approval in China

4. **Optimize/ streamline the evaluation and approval procedures** and accelerate approval for innovative drugs for urgent clinical needs. Increase CFDA /CDE's review and evaluation transparency

5. Carry out **the pilot programs of MAH** for new drugs for next 3 next years

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Highlighted issues

1. **New Drug Definition**: the drugs not yet marketed for distribution both within and outside the territories of PRC, is contradictory with International norms in Regulatory and IPR perspectives and could be a potential big risk for MNCs if NDA submission or approval is the cutting off date to be defined as New Drug category

2. The selling prices for new products in China are required **not higher than the prices** in countries of origin or neighboring comparable markets of China. CFDA needs to clarify the objective of requirement and to define "the selling prices"

3. **Methodology of quality consistent evaluation for Generics** need to defined clearly by CFDA, guideline announced for comments now.

4. “Licenses could be revoked if products haven't been marketed”. Ar renewal of license. This need CFDA to clarify further

5. Since this document is directional guidance, so **a set of implementation regulations are expected in near future**. Also, in accordance with rule of by law, the reform measures in this document should be put into the upcoming DRR revision and DAL revision to ensure appropriate implementation

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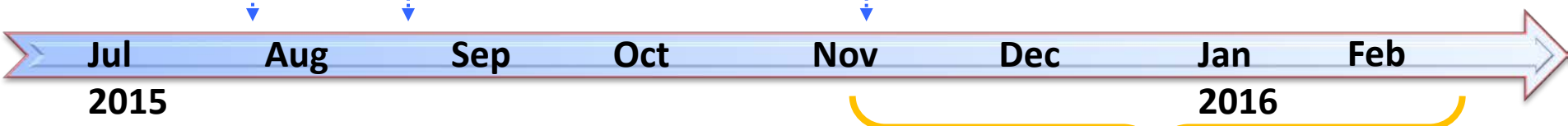
CFDA Roadmap for Implementation of No. 44 Document of the state council

- No. 117 & No. 140 from CFDA
- No. 44 from SC
- Pilot MAH and Drug Registration Category Reform approved by NPC LC (Nov 4th, 2015))



A set of implementing regulations released

- BE filing System for Chemical Drugs Registration
- Tech. Requirement for Registration
- Accelerating Evaluation & Approval of Innovative Drugs
- Priority Reviewing to Solve Backlog
- Chemical Drugs Registration Category

DRR /DAL Revision

A set of draft regulations or guidelines for commenting

- Draft Tech. Requirement for Registration
- Draft CDE working procedure for technical communication, reevaluation
- Draft Clinical Trials inspection procedure
- …..

- **No. 117 :** Clinical data integrity self inspection
- **No. 140**: Ten proposals to expedite registration review and approval
- **No. 44:** Opinions of the State Council on Reforming the Evaluation and Approval System for Drugs and Medical Devices

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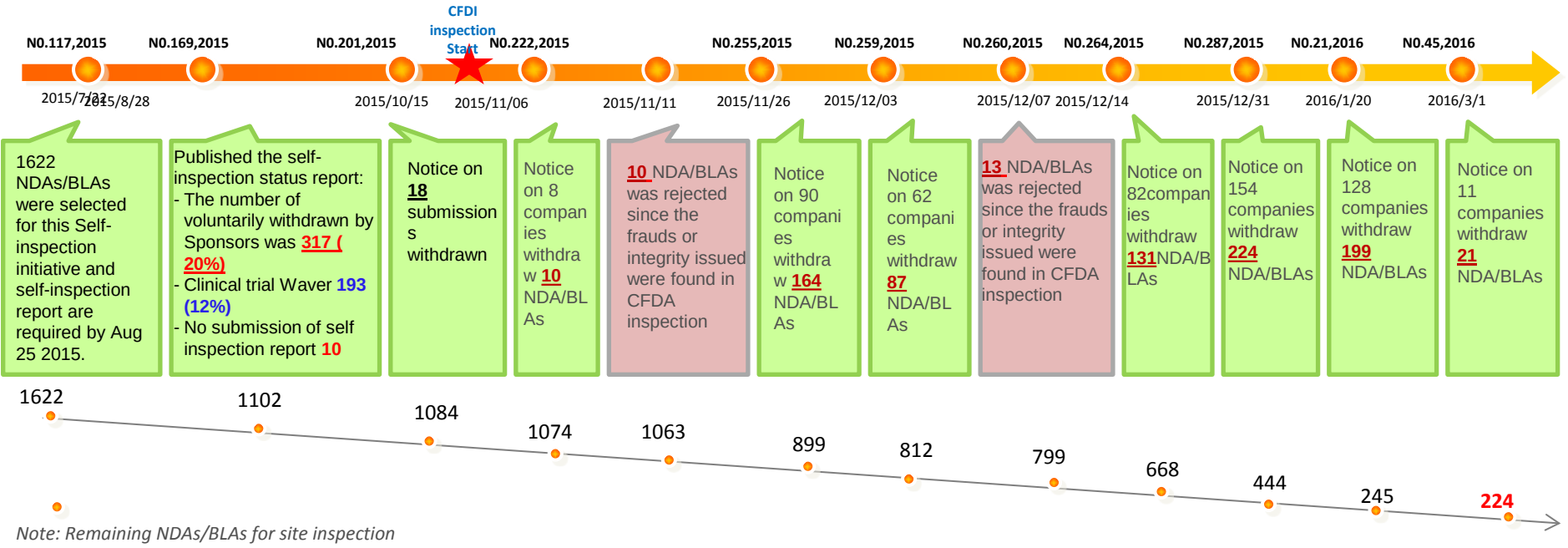
Inspection on clinical trials data: CFDA clean up the NDA/BLA with the **frauds and integrity** issues, ~85% was withdrawn by the applicants



Note: Remaining NDAs/BLAs for site inspection

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New Regulatory Regulations Formally Published in 1Q 2016

Feb 6
- The State Council opinion on implementing generic quality and efficacy consistency evaluation

Feb 20
- CFDA notice to suspend E-coding implementation and seek comments on GSP revision

Feb 26
- CFDA opinions on implementing priority review and approval to resolve the backlog of drug registration applications

Mar 4
- CFDA announced of chemical drug registration category reform

Mar 11
- State Council document No. 11 on Promoting Pharmaceutical Industry Sound Development – **Top-level design**

Positive

- ✓ Encourage Innovation
- ✓ Improve drug quality
- ✓ Resolve backlog
- ✓ Insist on "Four Strictest"

Still Remained Challenges:

- ✓ Cat. 5 without Monitoring period doesn't belong to "New Drug"
- ✓ Lack of tangible implementing and systematical coordination
- ✓ Need CFDA clarity the key uncertain areas

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Assessment of Chemical Drug Registration Category

Registration Category		Category Description	Monitoring Periods
New drugs	**1**	Innovative drugs not marketed at home and abroad	5 years
	2	New improved drugs that are not marketed at home and abroad	3-4 years
Generics	**3**	Imitation of **original drugs*** that are marketed overseas but unavailable domestically	NA
	4	Imitation of **original drugs*** that are marketed domestically	NA
Imported drugs	**5**	5.1 Application for the domestic marketing authorization of original drugs (both API and DP) marketed overseas	NA
		5.2 Application for the domestic marketing authorization of non-original drugs (both API and DP) marketed overseas .	NA

Undefined cut-off date of NDD

Need to define the tech. requirement clearly

Unclear benefits for MNC's

- No defined time point of qualifying New Drugs at CTA or NDA?
- Cat 5 of the originators
  - Lack of Regulatory data protection
  - Unclear impact on MA related policies about Cat. 5

Note:
***Original drugs :** the drugs marketed at home and abroad, owing complete and full data about safety and efficacy to get authorization.

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Assessment of Priority Review and Approval

Positive:

- Overall, it is a "Phased Regulatory Document" (阶段性注册文件), aiming to resolve the backlog of drug registration applications
- From the scope of the regulation, it covers both new drugs and Cat. 5 of originators for MNCs

Unclear Procedures need to seek CFDA's clarification:

Mainly including:

- Unclear expert panel criterion and working procedure
- Unclear timeframes for each step of the procedure e.g.
  - ✓ CDE technical review and supplement review
  - ✓ Inspection
- In NDA phase, it just specified for the local manufactured products. The imported NDAs need to clarify if to be covered

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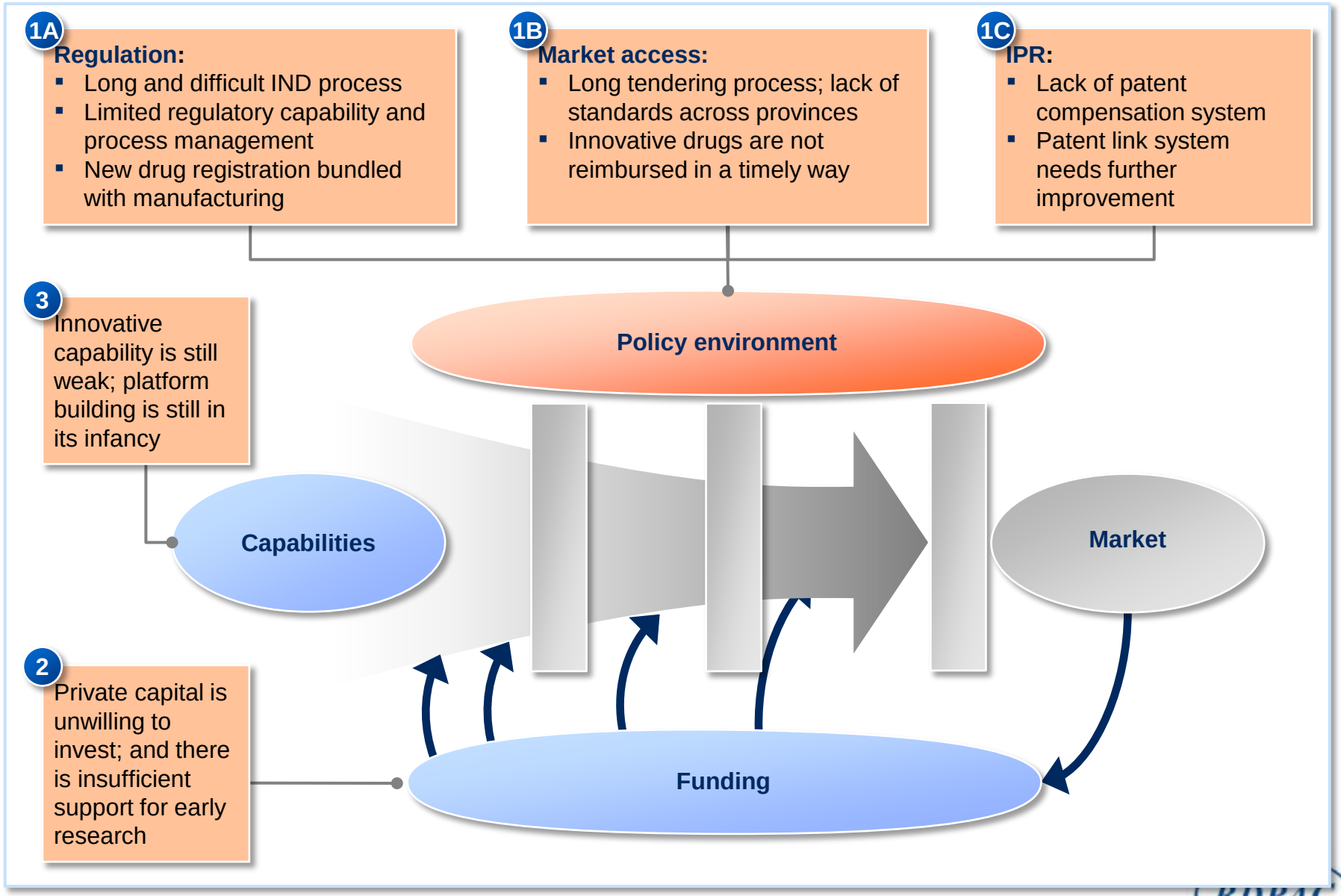
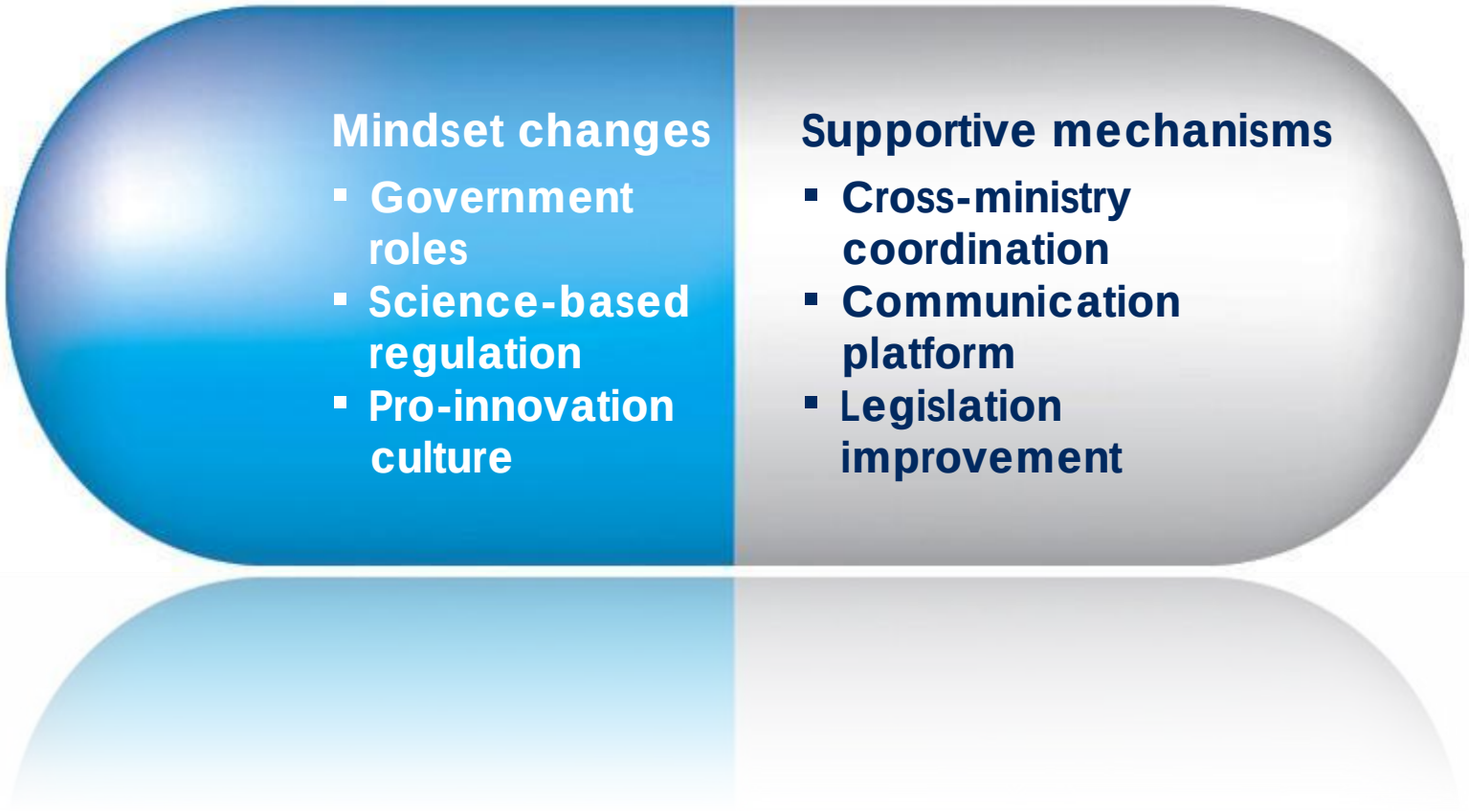
Challenges to China's drug innovation



Fostering a drug innovation ecosystem calls for mindset changes and supportive mechanisms



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Thank You !