Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

GMP for ATMPs

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Presentation outline

MHRA

Annex 2 - 2013

Change procedure for GMP guidelines

Part IV

EU & PIC/S

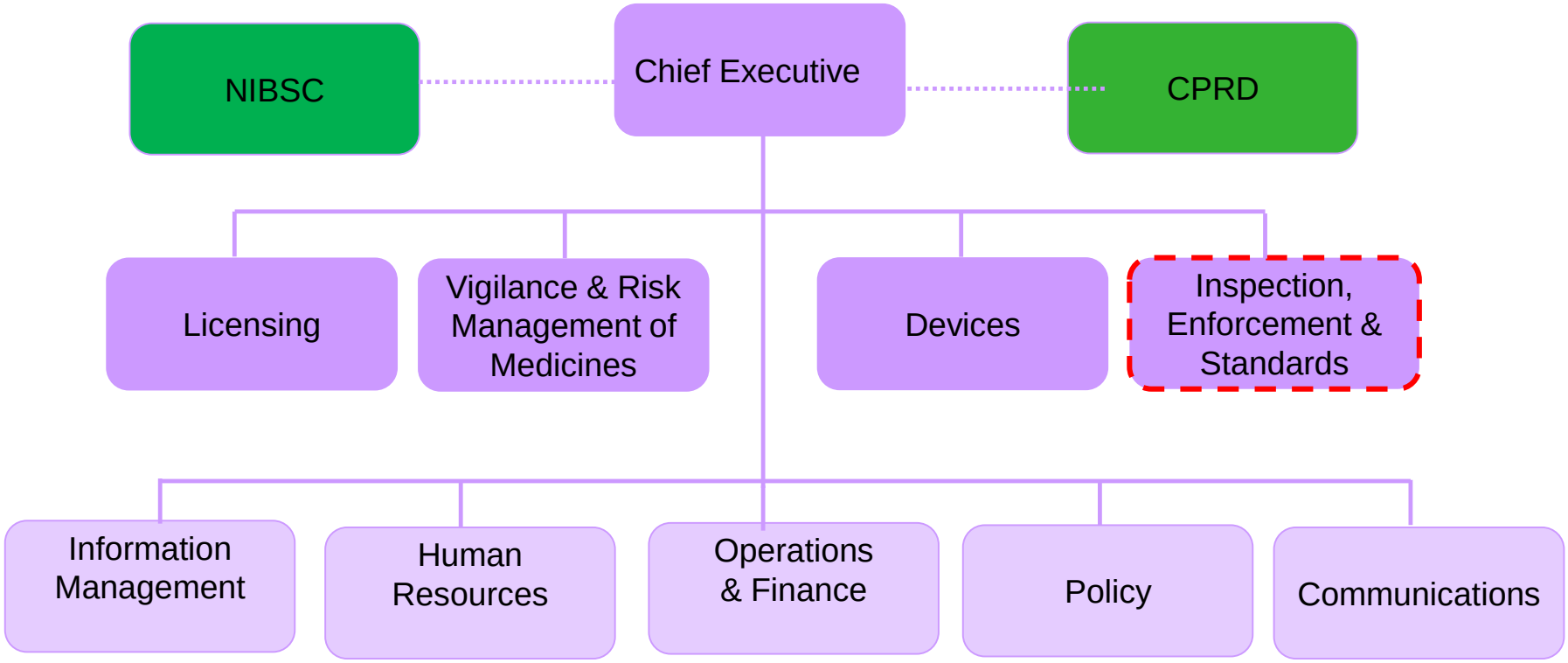
MHRA/BP/NIBSC - standards

Next steps

MHRA –Mission

We protect and improve the health of millions of people every day through the effective regulation of medicines, medical devices and blood, underpinned by science and research

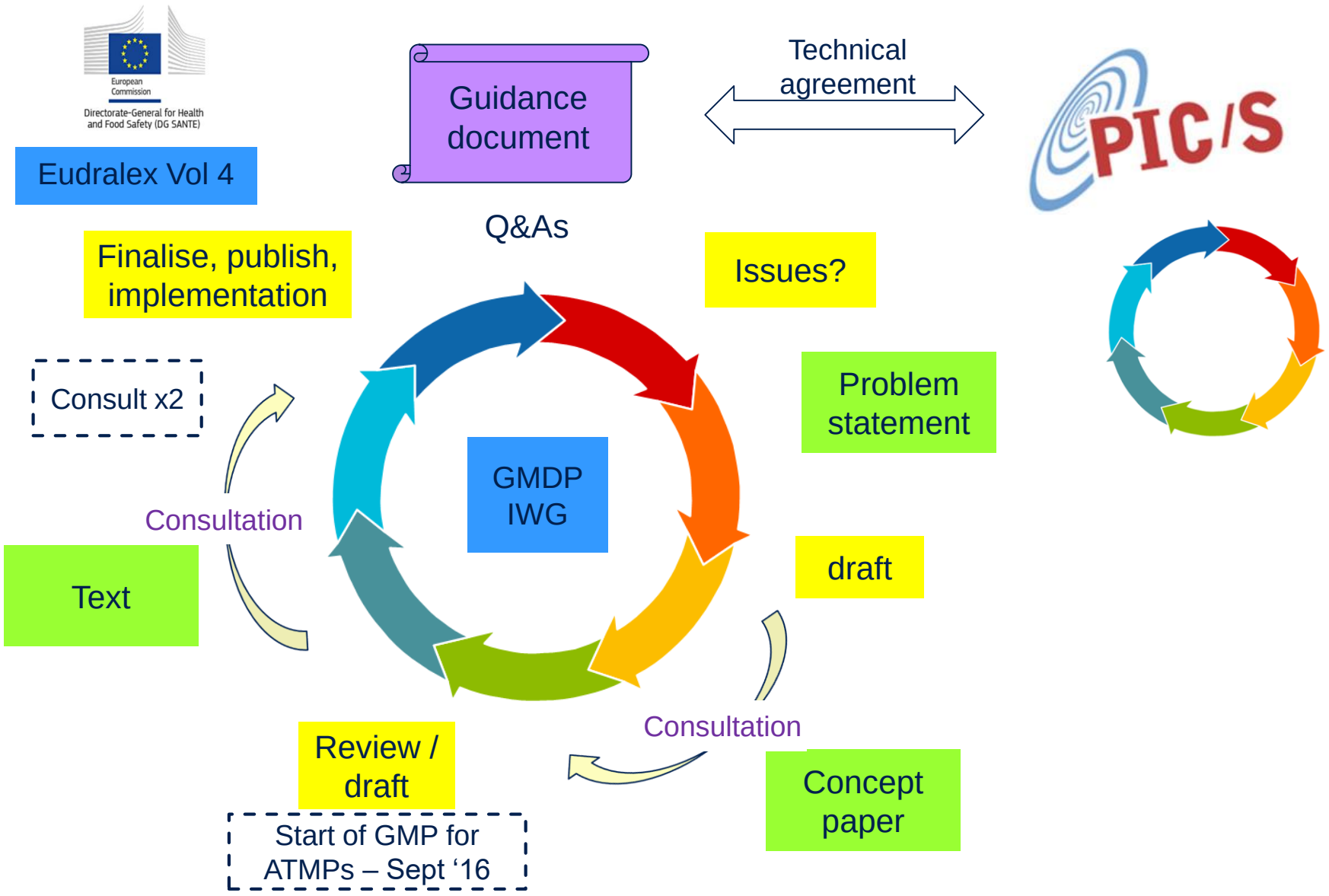
MHRA structure



EU GMP - biologicals: Annex 2

- Guidance on manufacture of biological medicinal products
- Written in early 1990's
- Revision in 2000's : General update, Science, technology, commercial practice, legislative changes – ATMP, blood, tissue and cells
- Article 5: 'The Commission shall, after consulting the Agency [EMA], draw up guidelines in line with the principles of good manufacturing practice and specific to advanced therapy medicinal products.'
- Drafting group: MHRA, IMB (HPRA), AIFA, PEI, AFSSAPS (ANSM)
- Came into effect Jan 2013

GMP change procedure - lifecycle



Part IV – timeline and adaptations

Came into effect in May ‘18, limited direct experience,

Annex 2 amended, came into effect in June ‘18

Inclusion of selected texts from Part I and annexes

New text on areas specific to ATMPS e.g.:

- 11.3.3 – point of care manufacture / decentralized manufacture
- 11.5 – administration of OOS products
- 11.15 – import of urgent / small volume products: no re-test
- 16 – reconstitution
- 17 – automated manufacture

Part IV: process

No involvement of Agencies / groups outside the EU

Part 4 is disconnected from all other areas of GMP:

- “These Guidelines are specific to ATMPs. Other documents developing GMP requirements for medicinal products which are contained in Volume 4 are not applicable to ATMPs, unless specific reference thereto is made in these Guidelines”
- Annex 1 – sterilization methods
- Annex 11 – validation of computer systems
- Annex 12 – ionizing radiation

Unclear maintenance system – for new topics / document revision

Part IV: document

Appears to give more flexibility, but gives less clarity which could lead to inconsistent interpretation:

- Manufacturers – many relatively new to medicines manufacture
- Inspectors – unclear
- Likely to need further interpretive documents to clarify

Reduced guidance on several areas:

- PQS e.g. change control, quality reviews, control of raw materials
- Appears to give hospitals and academia scope not to have an effective PQS
  - ‘different to conventional products’, ‘incomplete product knowledge’, ‘adjust manufacturing process’
  - Interpretational difficulties for a Risk Based Approach
    - little guidance on what this looks like

Part IV: document

Points to consider - Annex 1, general principles

“The manufacture of sterile products is subject to special requirements in order to minimize risks of microbiological contamination, and of particulate and pyrogen contamination. Much depends on the skill, training and attitudes of the personnel involved. Quality Assurance is particularly important, and this type of manufacture must strictly follow carefully established and validated methods of preparation and procedure. Sole reliance for sterility or other quality aspects must not be placed on any terminal process or finished product test.”

Part IV: document

Points to consider

- Annex 1 Working group transferred a lot of the draft details into the new ATMP guidance e.g. :
  - EM
  - Grade A/B/C and D
  - Gowning
  - Aseptic process simulation - media fill

Part IV: document

Points to consider:

Question: If agreed in an MA can a deficiency be cited in an inspection?

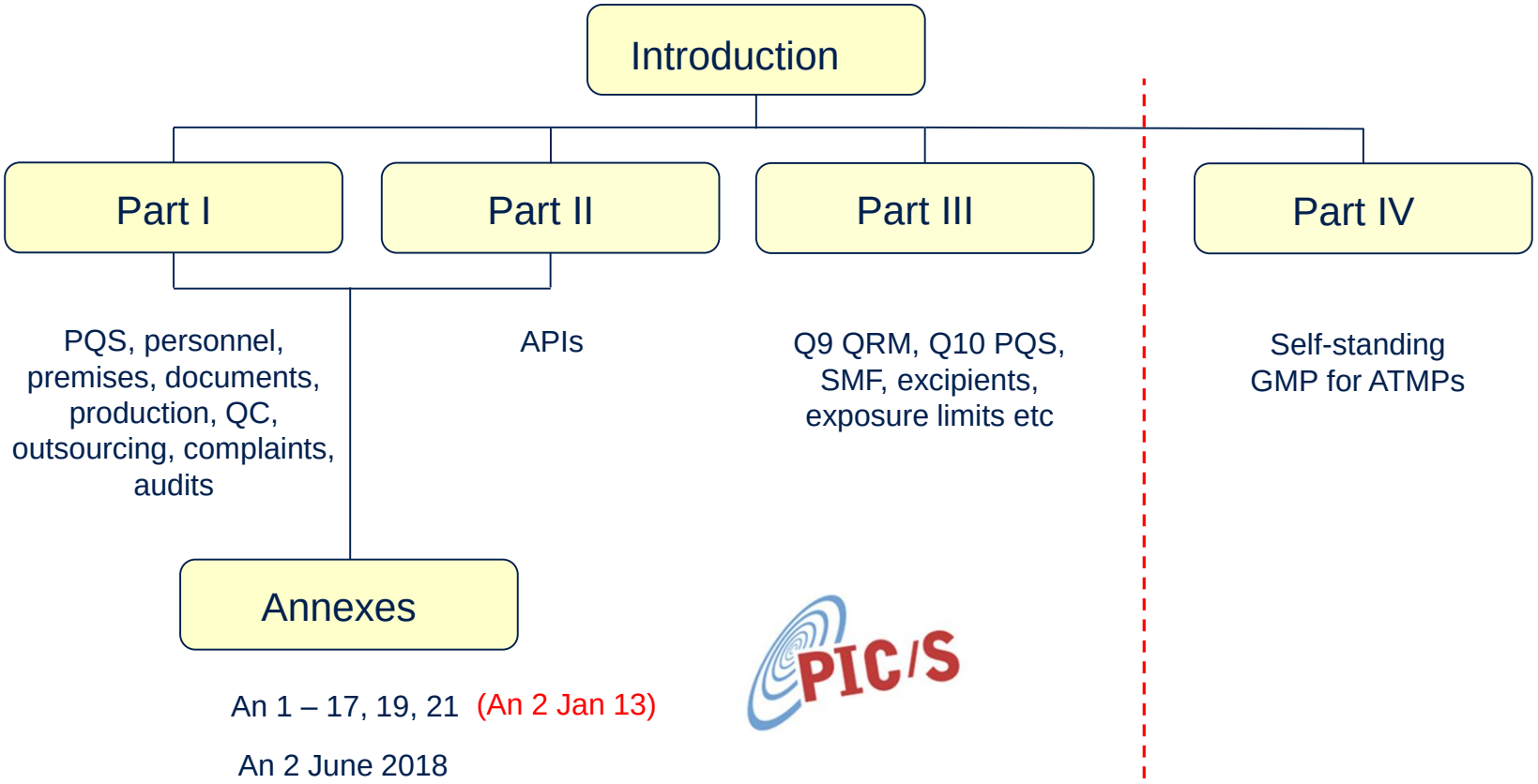
Part IV: document

Points to consider:

- 2.50 Allow flexibility of manufacture of early stage trials in A with C background in “exceptional” circumstances

Question: What do you think exceptional circumstances are?

GMP guidance - EU and PIC/S



Next steps: PIC/S ATMP guidance

- Started in 2016 to discuss issues with the Commision:
  - Canada (lead)
  - Australia
  - France
  - Indonesia
  - Italy
  - Ireland
  - Japan
  - Republic of Korea
  - Malaysia
  - Netherlands
  - Sweden
  - Spain
  - Switzerland
  - UK
- Differences in GMP guidelines created
  - Does not have Part IV, Annex 2 at previous (2013) version
- Drafting group
  - TGA lead, members – MHRA, AIFA, HPRA, Swissmedic, Chinese Taipei
  - Problem statement completed, guidance text being drafted
  - Propose to create guidance within the GMP annexes
  - No need to re-state texts from Part I, III or annexes, keep QRM etc

Next steps – GCP

- ATMP regulation:
  - Article 4(2). The Commission shall, after consulting the Agency, draw up detailed guidelines on GCP specific to ATMPs.
- At consultation 1st August - 31 October 2018
- Outcome will be different
  - GCP for ATIMP will supplement ICH's E6 GCP Guideline

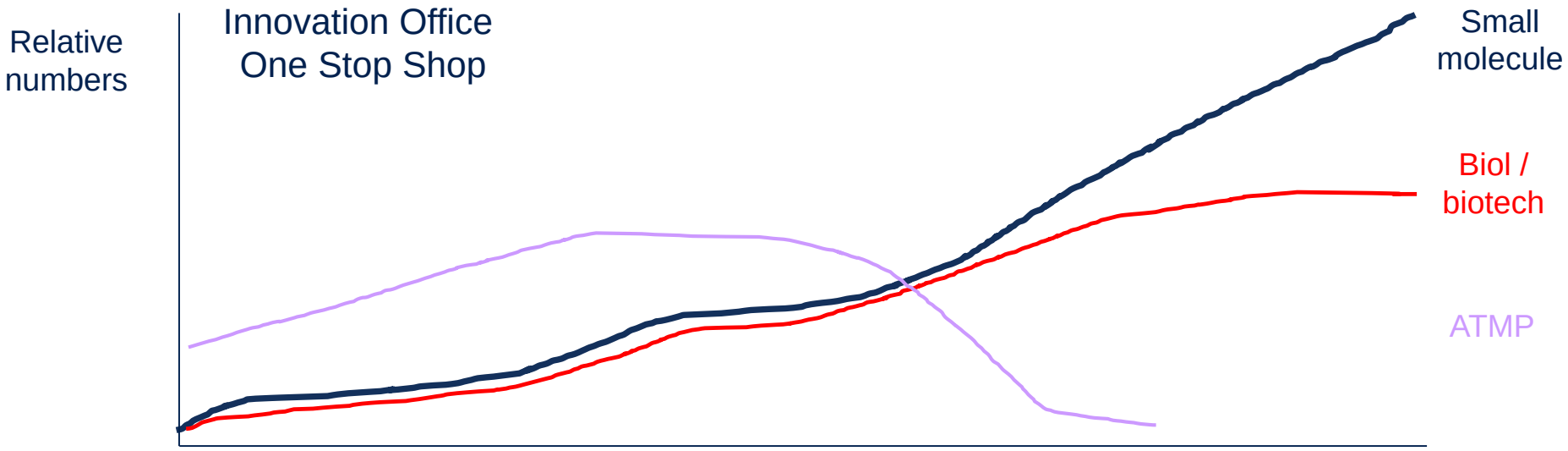
MHRA strategy - Pharmacopoeial Standards for Biological Medicines

- Consultation early 2017
  - quality and support for innovation
  - IO / OSS / EAMS
  - Implement ATMTF recommendation on standards
- Adopted October 2017
- Key themes:
  - Supporting innovation
  - Collaboration and engagement
  - Mutual knowledge building

https://www.gov.uk/government/consultations/strategy-for-pharmacopoeial-public-quality-standards-for-biological-medicines

MHRA strategy - Pharmacopoeial Standards for Biological Medicines

Discovery | Preclinical | Clinical trials | Marketing authorisation | Widespread adoption



MHRA strategy - Pharmacopoeial Standards for Biological Medicines

Work to achieve this strategy:

- Engagement with wider community
- Working to establish a specialised ATMP working party
  - Informal stakeholder workshop being developed to discuss standards and the most valuable areas to target
  - Become involved - please contact: alistair.gibb@mhra.gov.uk and alice.gardiner@mhra.gov.uk

New products

- MAs being granted
- Not all have been given a positive cost / benefit opinion by NICE

Early engagagement!

- IO / RASRM (OSS) for regulatory advice
- CT Unit / Licensing Division for scientific advice

Thank you for your attention

Questions?