Stakeholder education on biosimilar concepts - why does it matter globally?

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Stakeholder education on biosimilar concepts

• What is the purpose?
• How far have we come?
• Critical issues, critical steps
• Lessons from Europe? *Think globally, act locally*
Stakeholder education on biosimilar concepts

**Stakeholder Education - what is the purpose?**
Knowledge where it is needed

“Knowledge is of two kinds. We know a subject ourselves, or we know where we can find information upon it.” – Samuel Johnson

Boswell’s Life of Samuel Johnson (1791, vol 2), April 18, 1775, p. 258.

• We know a subject…
  – Stakeholders look for parallels to what they already know
  – Generic concept vs. biosimilarity

• We know where to find information…
  – Different capacity and familiarity across stakeholder groups
  – Typically look to their regular sources for information
  – Interpret information differently
    • Bias
    • Meaning

• For all, it is a process rather than an event
Stakeholder education

- **Science and society**\(^1\) – mutual understanding with scientists playing the role of coach or supporter

- Engagement requires
  - Information
  - Communication
  - Knowledge in context (practical and social)\(^2\)

- Recent research on science and society\(^1\)
  - Engagement on genomics research
  - Stakeholders from different backgrounds in the Netherlands

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“For participants, knowledge is still considered an important factor in this communication process, and informing the public is appreciated. Yet communication entails more than information dissemination. Participants in various roles emphasise the importance of informing people by various means. In all roles participants consider transparency and openness important conditions for people’s trust in this information.”

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How far have we come?
Stakeholder engagement – building momentum

- Familiarity of biosimilarity concepts moving slowly
  - Concern that this could be limiting uptake
- DG Enterprise – Platform on Access to Medicines Initiative
  - “invited to take stock of the availability of biosimilar medicinal products in European national markets and to define the necessary conditions for an informed uptake and adequate patient access to these products.”¹
  - Consensus documents
  - Still building a readership for these
- Regulators reaching out to clinicians
  - Articles
  - Presentations and conferences
- WHO similar biotherapeutic products guidelines and training

¹ [Link](http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/process_on_corporate_responsibility/platform_access/index_en.htm#h2-6); accessed March 1, 2014
Engaging with biosimilars: pharmacists taking a lead

- Pharmacists reaching out to better understand formulary choices and conditions
- Vanguard stakeholders vis-à-vis biosimilars
  - First requests a few years ago
- Now important translators of the concepts to clinical practice
  - Can play an important role for all healthcare providers
Engaging with biosimilars: clinicians

- Surveys to date show areas for further engagement
- Two recent surveys: ASBM, AIOM
- **ASBM survey** across disciplines, 5 countries (UK, F, D, I, E)
  - Still working on familiarity with biosimilarity
    - Just over 50% felt that they had a basic understanding
    - 25% full understanding vs 25% limited/none
  - Implications for prescribing less clear
    - 37% did not understand that extrapolation of indications is possible
    - 61% thought the same non-proprietary name meant that a biosimilar would have approval for all the same indications of the reference medicine
      - 39% thought that the same non-proprietary name also mean that patients could be safely switched during treatment with the same results
  - Concerns about prescriber control
    - Even at selection of a biologic on initiation of treatment (62% not acceptable for a pharmacist to make this decision)
Engaging with biosimilars: clinicians

- Oncologists in Italy
  - Survey 2013
  - 858 members
  - Nov – Dec

- Evidence that familiarity of biosimilars achieved, but more to do for understanding and confidence-building
  - 79% of respondents could correctly define biosimilars compared with 24% in an earlier survey

http://www.biodrugsnews.net/farmaci-biosimilari.php; accessed March 1, 2014

http://www.biodrugsnews.net/pdf/sondaggio_tappe.ppt; accessed March 1, 2014
Clinicians: concerns and context

AIOM Survey 2013 – Oncologists in Italy

• Survey signals areas of focus
  – Relevant differences between the reference medicine and the biosimilar
  – Selection of clinical end points, clinical design
  – Potential for uncontrolled trade via the internet
  – Extrapolation:

• For 88% of respondents, the decision to switch between a biosimilar and its reference product should remain with the prescriber

http://www.biodrugsnews.net/pdf/sondaggio_tappe.ppt; accessed March 1, 2014
Engaging with biosimilars: patients

• Until recently, limited engagement of patient groups in the debates
• Many patient groups are now exploring biosimilars
• International Alliance for Patients’ Organizations has been a pioneer
Patients setting their own terms for engagement

- International Alliance for Patients’ Organizations (IAPO) updates its 2006 paper with a comprehensive toolkit in 2013
  - Surveyed key areas for engagement for patients

International Alliance of Patients Organization, Briefing Paper on Biological and Biosimilar Medicines (2013) p. 16
Still to engage…

• Need for user-defined training and engagement
  – Less “push”….more “pull”

• Nurses
  – Care teams
  – Critical translator for patients
  – Very limited engagement so far

• Wider public
  – Media / press coverage has been limited and often focused on the business interests
  – Some coverage even misleading about biosimilar concepts, although improving
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CRITICAL ISSUES, CRITICAL STEPS
Interchangeability – not a single definition

International, interdisciplinary confusion

• Not always a singular meaning, interpretation

Interchangeability: The medical practice of changing one medicine for another that is expected to achieve the same clinical effect in a given clinical setting and in any patient on the initiative, or with the agreement of the prescriber.

Substitution: practice of dispensing one medicine instead of another equivalent and interchangeable medicine at the pharmacy level without consulting the prescriber.

Interchangeability, Substitution and Switching

• Interchangeability - Health Regulatory Authority Designation
  - US FDA: Expected to produce the same clinical result as the reference product in any given patient; and repeated switching between biosimilar and reference product presents no greater safety or efficacy risk than continued use of the reference product.
  - WHO: pharmaceutical product is one that is therapeutically equivalent to a comparator product and can be interchanged with the comparator in clinical practice.

• Substitution – Pharmacist Action
  - When a pharmacist substitutes a certain prescribed product by another equivalent product.
  - If without the prescribing physician’s knowledge, it is considered “automatic” or “involuntary” substitution.

• Switching - Treating Physician Decision
  - When a prescribing physician changes medication.
Interchangeability, substitution, switching

- Considerable confusion between these concepts and terms of use
  - Work underway in some Member States (Italy, France)
- At core is an understanding of under what terms a medicine can be replaced for another
  - Biosimilar vs. reference, biosimilar vs. biosimilar, reference vs. another originator
  - When in a care pathway?
  - Who takes the decision and responsibility (clinician, pharmacist)?
  - With what scientific evidence to support the decision?
- Media often conflates the concepts, assumes an approach
  - Generics experience again used as an analogy
  - Biosimilars have a distinctive regulatory pathway, and accordingly they will have a distinctive market development
Extrapolation of indications: understanding the basis

- Explanations focus on the regulatory requirements
  - Extrapolation to be scientifically justified on a case by case basis
- Technical definitions do not always translate


International Alliance of Patients Organization, Briefing Paper on Biological and Biosimilar Medicines (2013) p. 10
Extrapolation of indications – understanding the outcomes

- Predictability comes from understanding the decision making process
- Challenge where decisions appear to be made on different terms or where different determinations result

Regulatory Note

Is Extrapolation of the Safety and Efficacy Data in One Indication to Another Appropriate for Biosimilars?

Howard Lee¹,²

Received 31 July 2013; accepted 19 September 2013

Abstract. CT-P13, the world’s first biosimilar monoclonal antibody to infliximab, was approved to marketing in South Korea for all the six indications of infliximab, which Europe may follow, although the product was tested only in rheumatoid arthritis (RA) with a limited pharmacokinetic comparison in ankylosing spondylitis. However, the extrapolation of the efficacy and safety findings of CT-P13 in RA to the other indications appears scientifically challenging when assessed by the current regulatory requirements. RA is not a sensitive clinical model to detect potential differences between CT-P13 and infliximab, and other mechanisms of action than antagonizing tumor necrosis factor α appear to be also important, which could be different by the approved indications. Furthermore, the immunogenicity and safety profiles of CT-P13 were not sufficiently characterized in that immunogenicity potential was lower in RA, which was even further suppressed by the concomitant use of methotrexate. Extrapolation of the safety and efficacy data in one indication to another may be inappropriate for biosimilars unless backed up by strong scientific justification, which may include the mechanistic exposure-relationship approach. Therefore, regulatory agencies need to exercise caution before granting extrapolated indications for biosimilars.

KEY WORDS: biosimilars; CT-P13; extrapolation of indication; infliximab; regulatory agency.
Explaining extrapolation

• Understanding the definition is not enough
  – For many stakeholders, the definitions do not clarify the meaning
  – Underlying science needs to be explained

• Science underlying the principle is in debate

• As with all scientific discourse, the only way forward is full engagement in outlining and testing the principles
  – Presumes that participants have a similar core knowledge
  – That may not be valid

• Explaining extrapolation is a critical step in stakeholder engagement

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LESSONS FROM EUROPE?
Think globally, act locally
Building knowledge and understanding

- Engage in the dialogue
  - Open and transparent
  - Invite more voices
- Questions about the basis for regulatory licensure and biosimilars development are an invitation to engage
- Support stakeholders’ efforts to make sense of biosimilarity concepts themselves

Building knowledge and understanding

• Answer the questions
  – Let stakeholders ask the questions
    • Consensus Document Q&A
  – Timing and relevance
    • Role dependent
    • When they need to know

• Conclusions for action:
  ➢ User-defined information, communications, training
  ➢ Need to consider timing – when is the right time?
  ➢ A process rather than an event
  ➢ Global understanding will build on EU foundations of strong
    stakeholder engagement

“Therefore, changing roles, for example, when people become patients, can affect the urgency for information and the urgency to participate.”