# Professor Dr İbrahim C Haznedaroğlu, MD, Turkey

- Clinical Professor of Medicine and Hematology, Hacettepe University Medical School, Turkey

**GaBI Educational Workshops**

First Turkish Interactive Workshop on Regulation and Approval of
SIMILAR BIOTHERAPEUTIC PRODUCTS/BIOSIMILARS

2–3 March 2016, Hacettepe University, Ankara, Turkey

# Current regulatory approval standard and practice on biosimilars

Professor Dr İbrahim Haznedaroğlu, MD

2 March 2016

GaBI
GENERICS AND BIOSIMILARS INITIATIVE
*Building trust in cost-effective treatments*

HACETTEPE UNIVERSITY

PPCI
Pro Pharma Communications International

# Current regulatory approval standard and practice on biosimilars

**Ibrahim C. Haznedaroglu, MD,**

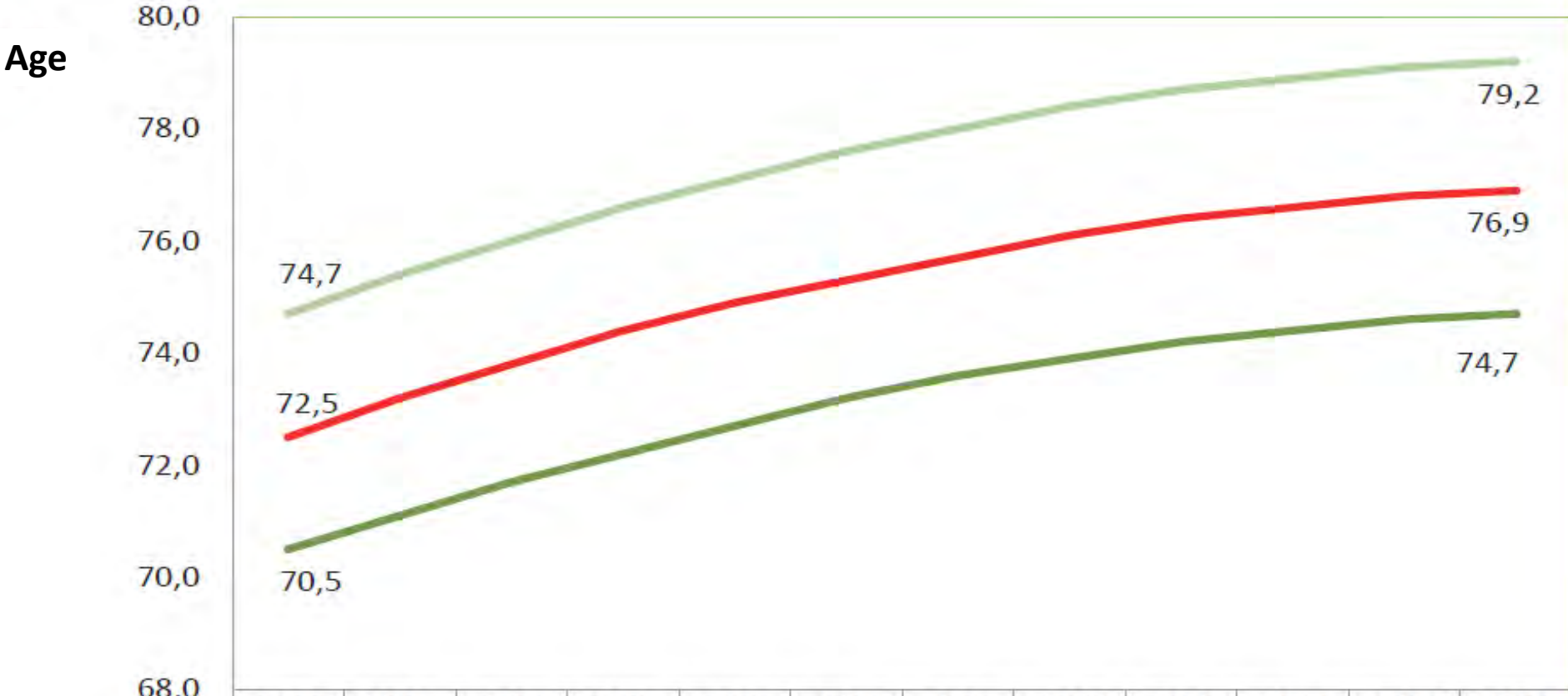
**Hacettepe University Medical School**

**Department of Haematology, Ankara-Turkey**

# Turkey

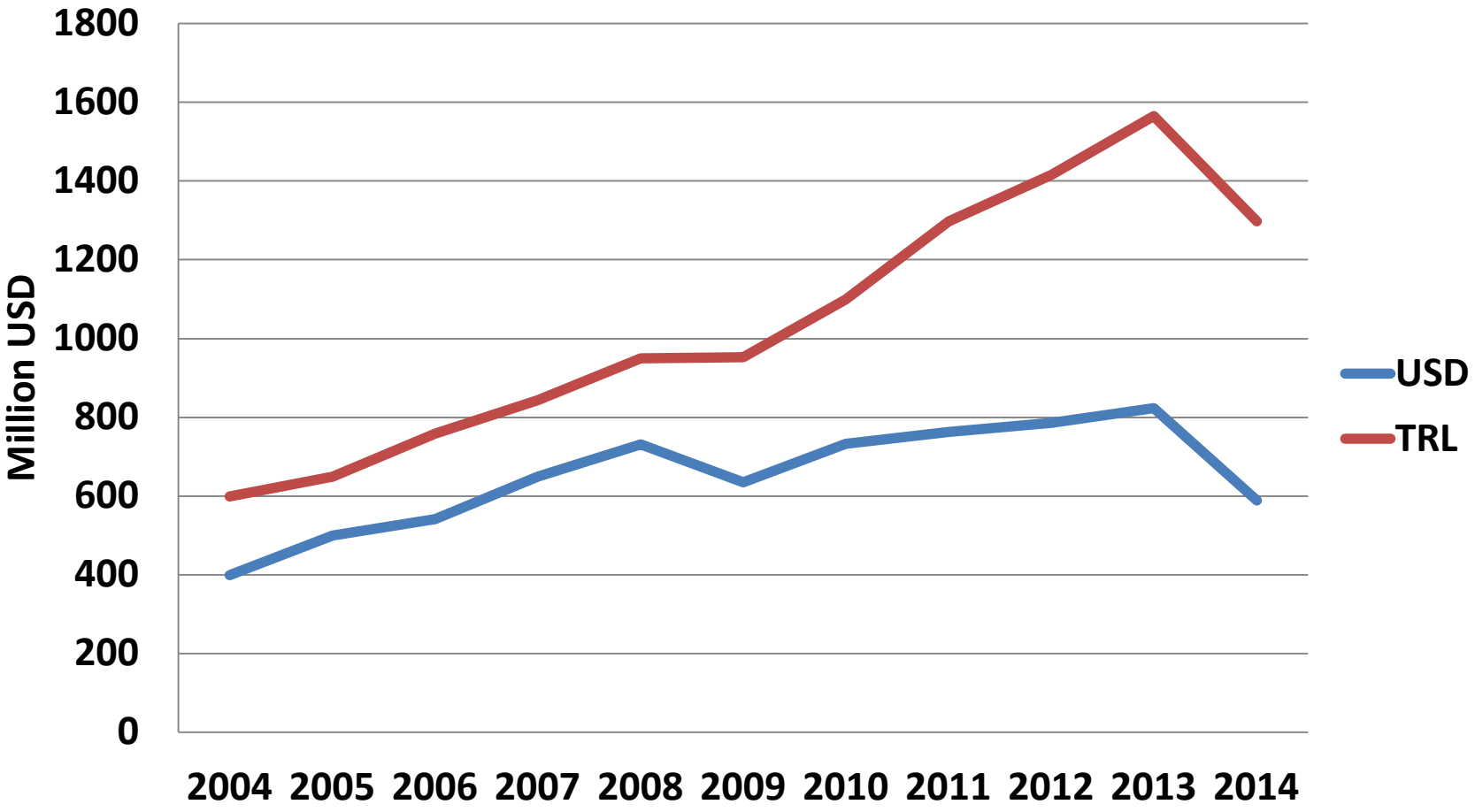
- Population: 77 million
  - ¼ of the population is < 14 years of age (EU 15%)
  - 11% of the population > 60 years of age (EU 23%)

# Life Expectancy at Birth - Turkey

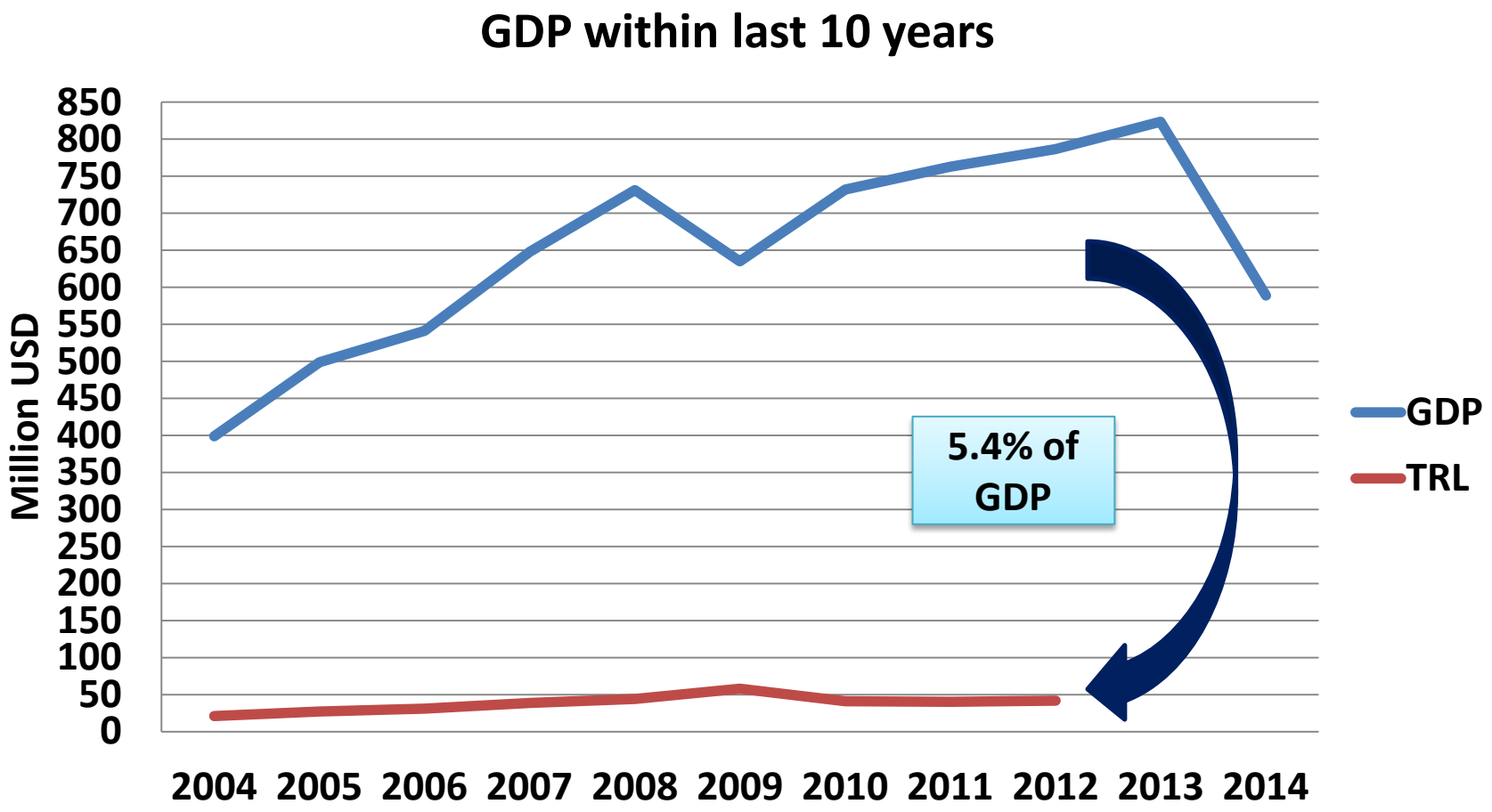



| | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Male | 70,5 | 71,1 | 71,7 | 72,2 | 72,7 | 73,2 | 73,6 | 73,9 | 74,2 | 74,4 | 74,6 | 74,7 |
| Total | 72,5 | 73,2 | 73,8 | 74,4 | 74,9 | 75,3 | 75,7 | 76,1 | 76,4 | 76,6 | 76,8 | 76,9 |
| Female | 74,7 | 75,4 | 76 | 76,6 | 77,1 | 77,6 | 78 | 78,4 | 78,7 | 78,9 | 79,1 | 79,2 |

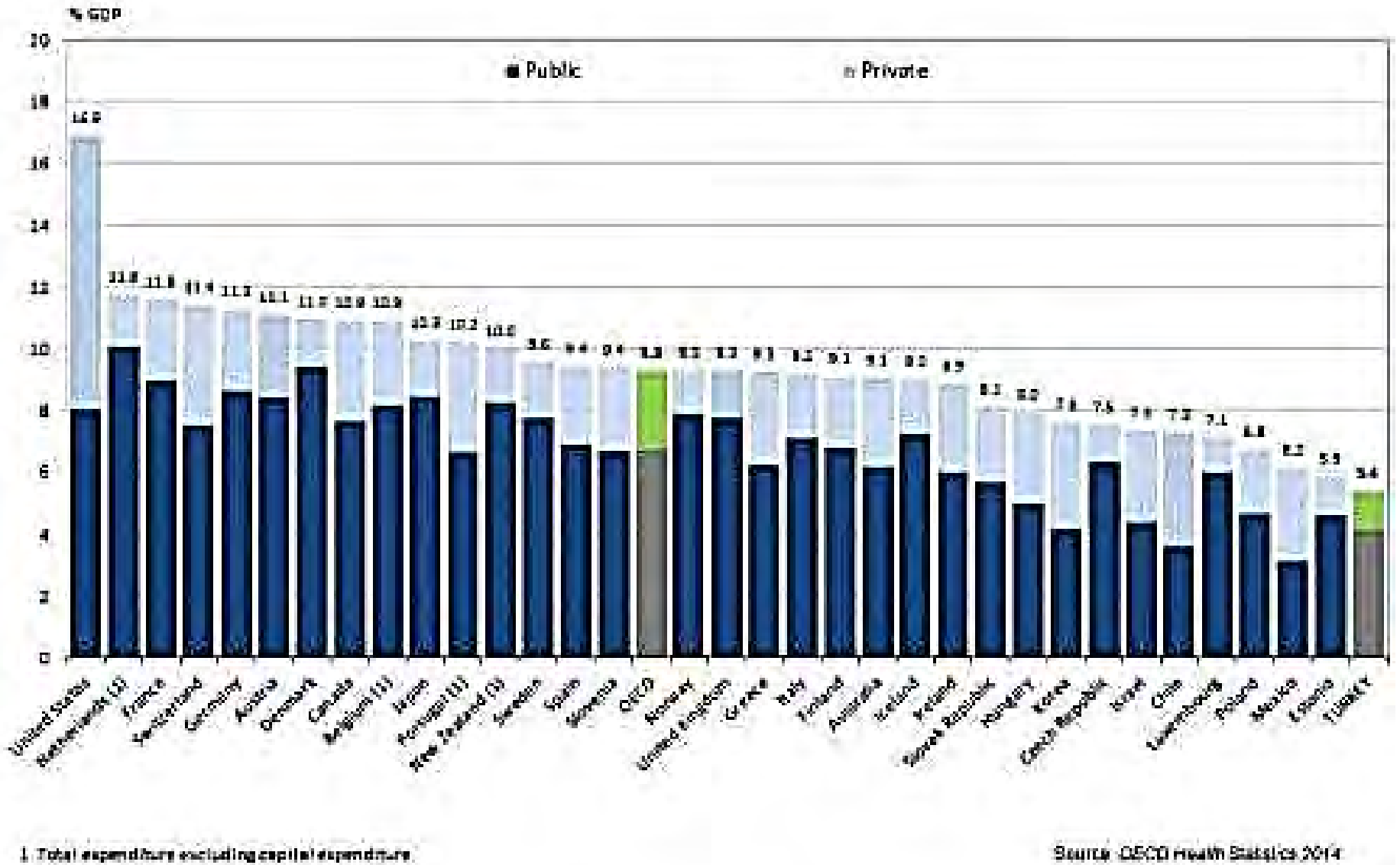
# Gross Domestic Product in Turkey



# Total Healthcare Expenses



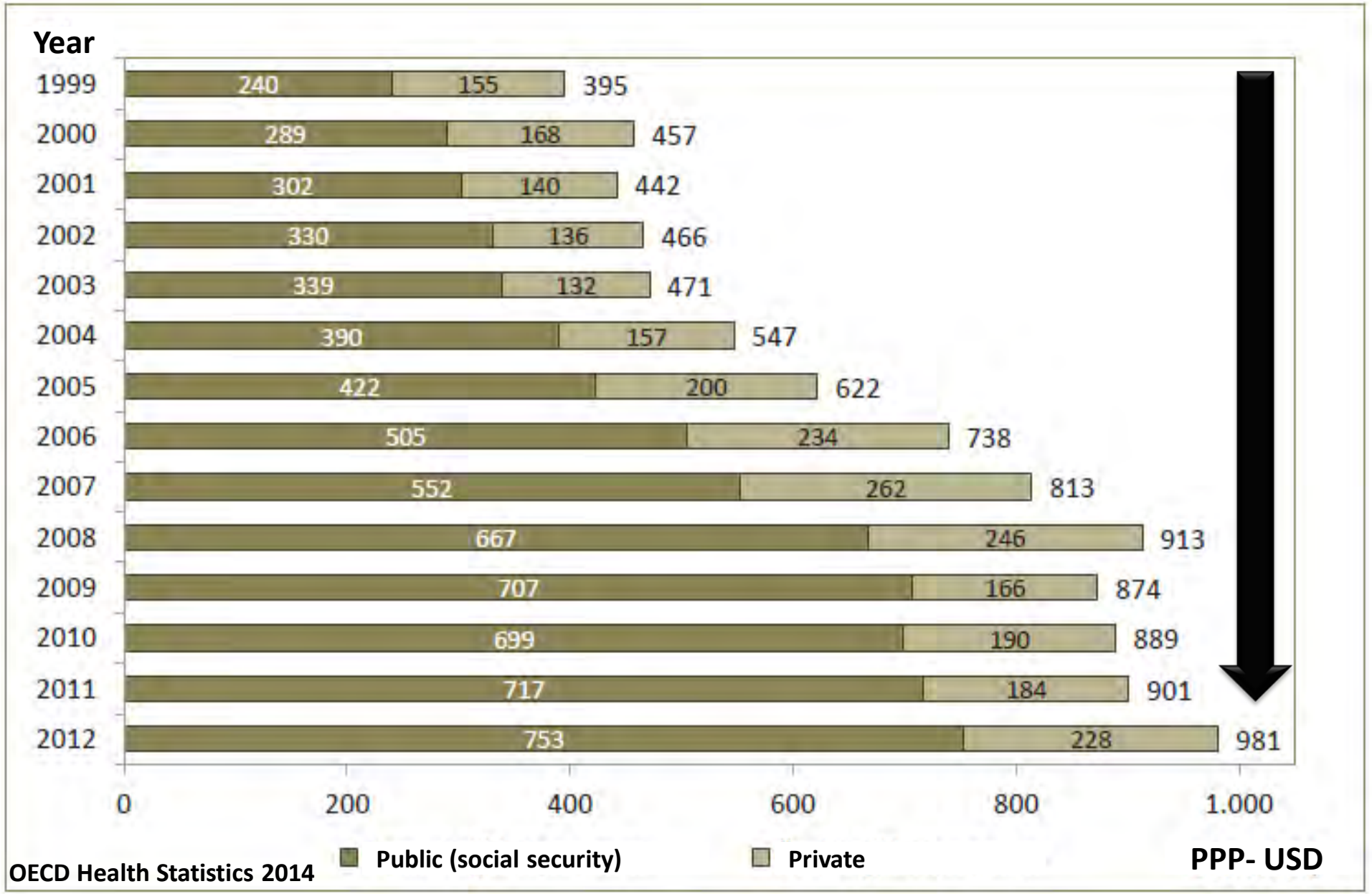
# Total Health Expenditure as of GDP% - OECD




1. Total expenditure excluding capital expenditure

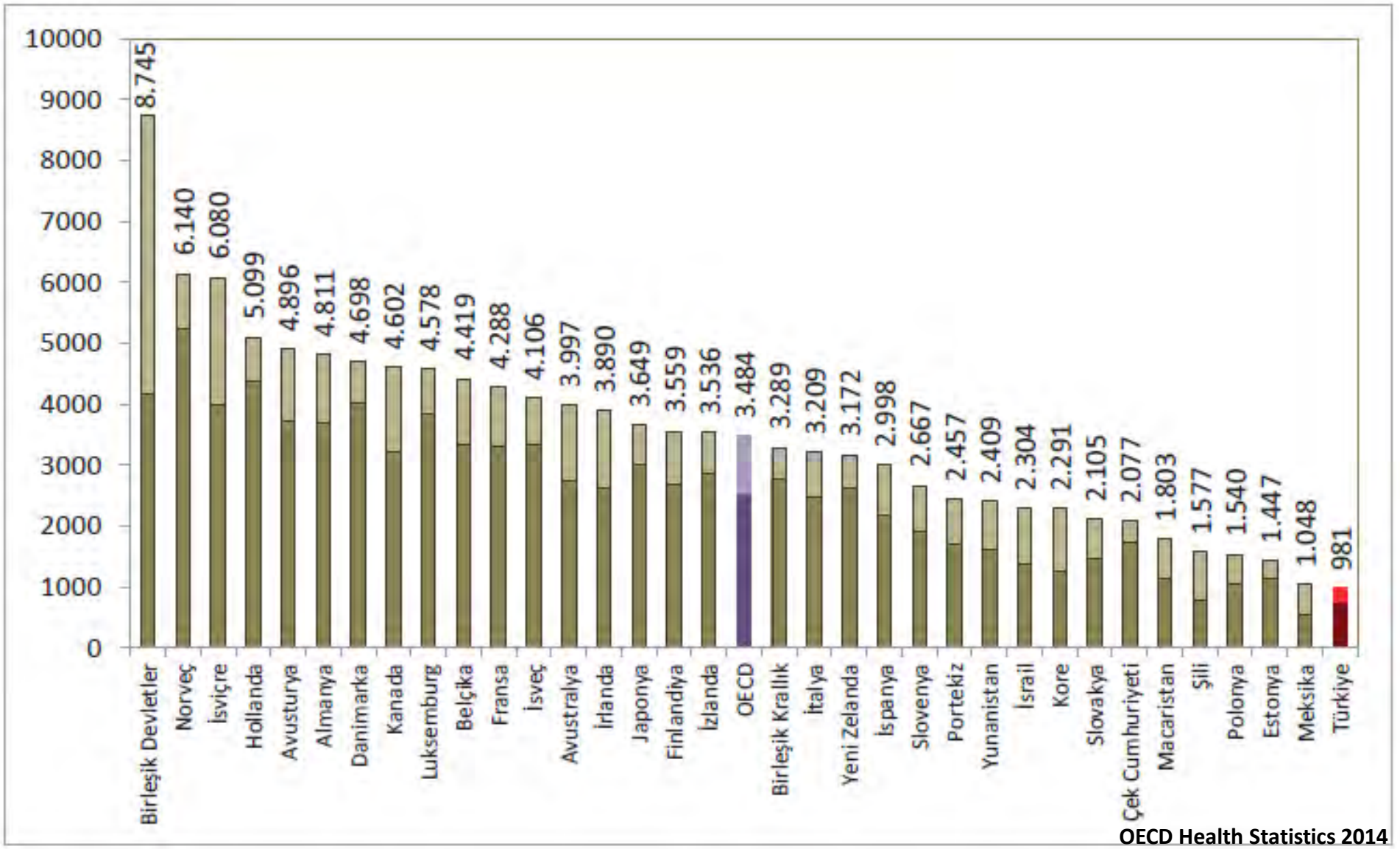
Source: OECD Health Statistics 2014

# Per Capita Health Expenditure - Turkey



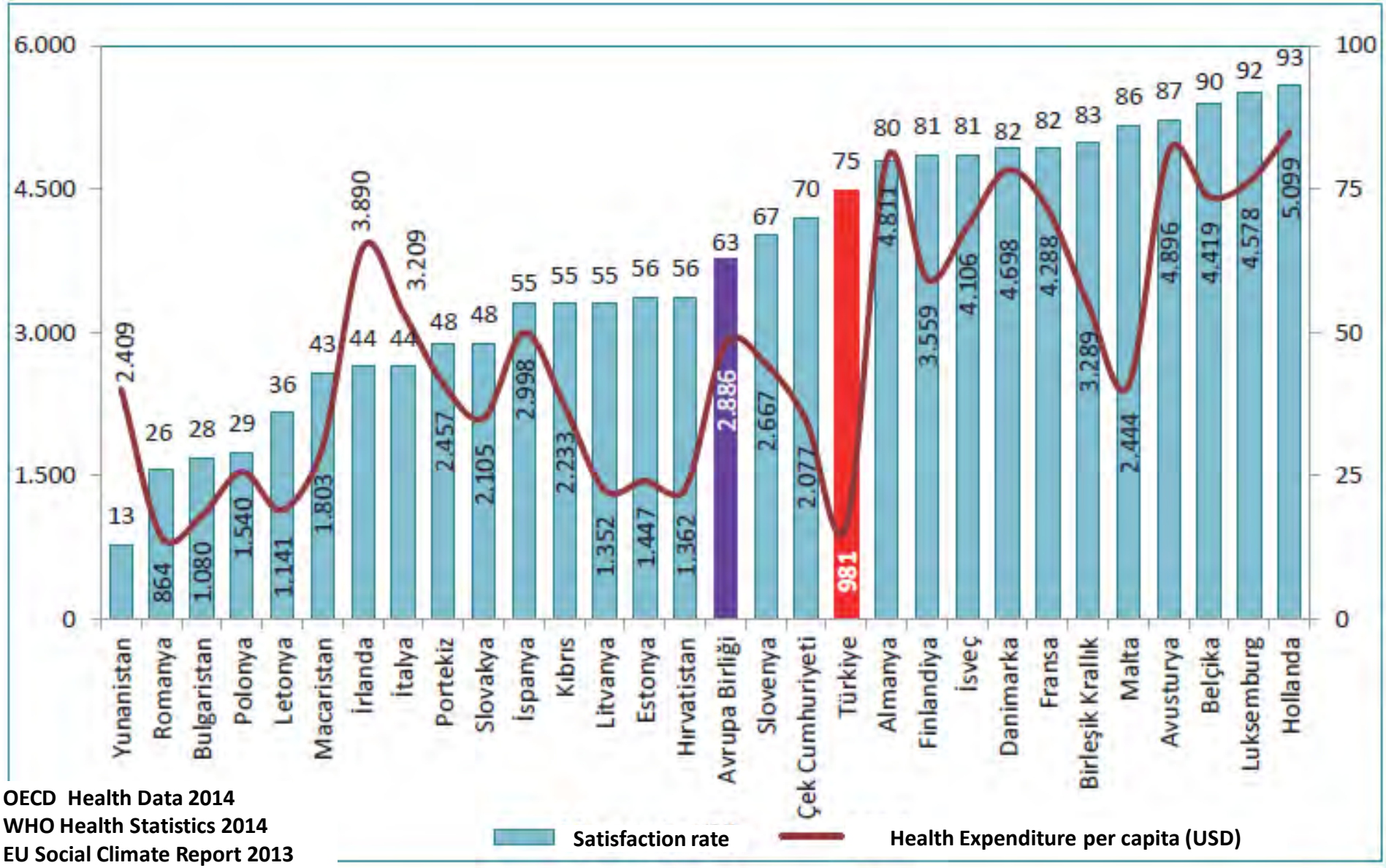
# Per Capita Health Expenditure - OECD

**PPP- USD**

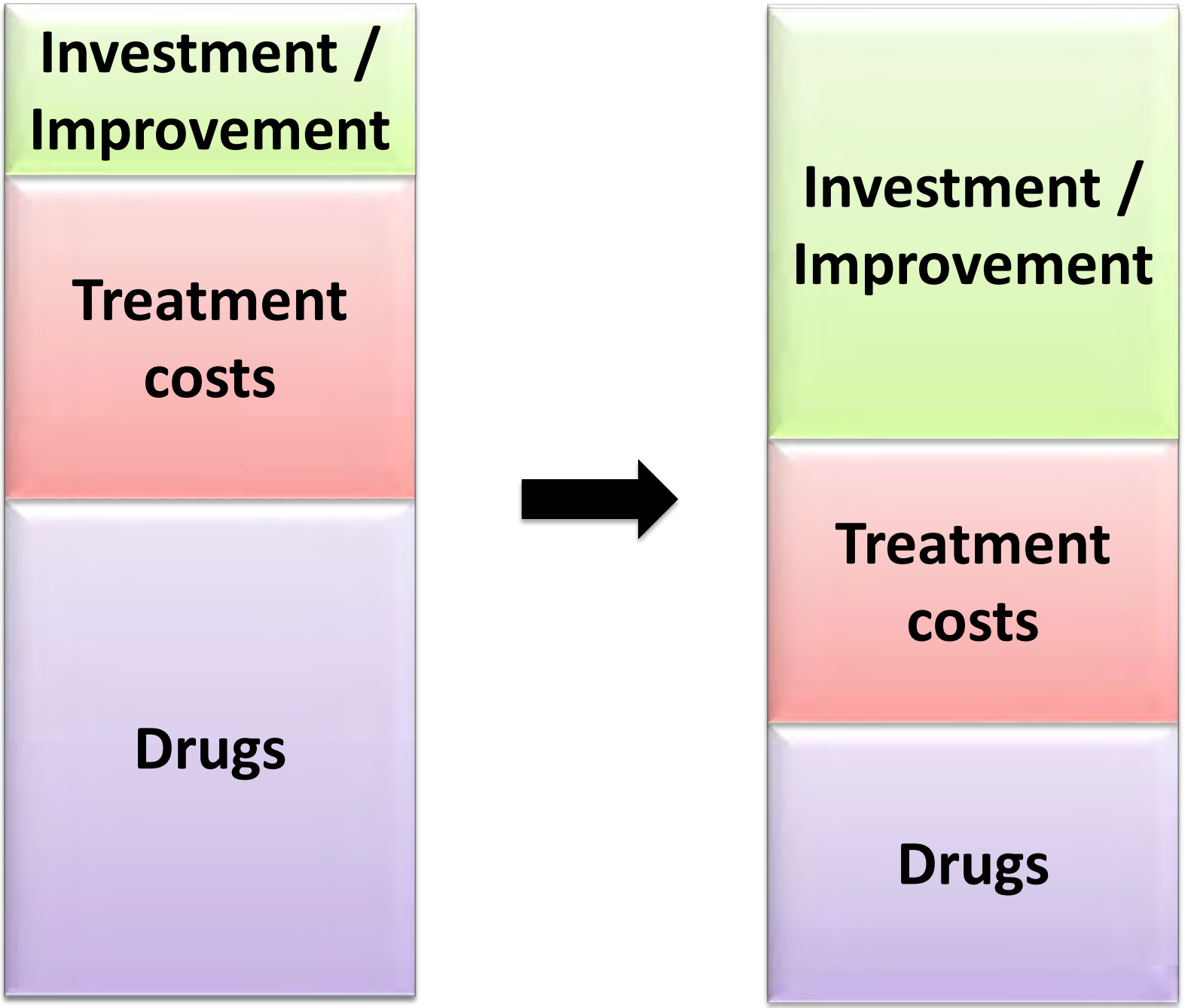



OECD Health Statistics 2014

# Total Health Expenditure (per capita - USD) Satisfaction Rate in Healthcare Services




OECD Health Data 2014
WHO Health Statistics 2014
EU Social Climate Report 2013


Investment / Improvement
Treatment costs
Drugs
Investment / Improvement
Treatment costs
Drugs

# Results

- Quality of healthcare improved
- Access to medicine enhanced
- Access to technology/modern treatment and diagnostic modalities increased
- Satisfaction increased

# Access to medicine enhanced Satisfaction increased

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

OCTOBER 1, 2015

INTERNATIONAL HEALTH CARE SYSTEMS

## Transforming Turkey's Health System — Lessons for Universal Coverage

Rifat Atun, M.B., B.S., M.B.A.

In 2003, Turkey embarked on ambitious health system reform to overcome major inequities in health outcomes and to protect all citizens against financial risk. Within 10 years, it had achieved universal health

(HTP) that aimed to improve public health, provide health insurance for all citizens, expand access to care, and develop a patient-centered system that could address health inequities and improve out-

INTERNATIONAL HEALTH CARE SYSTEMS

# Transforming Turkey's Health System — Lessons for Universal Coverage

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## MYOCARDIAL INFARCTION

*A 55-year-old man with no other serious health conditions has a moderately severe myocardial infarction.*

Chest pain and breathlessness develop during the day in Mr. Öztürk, a civil servant who lives in a large city. His family calls an ambulance, which arrives within 10 minutes. He is assessed by the paramedical staff and stabilized with oxygen and painkillers. His electrocardiogram indicates a myocardial infarction. He is taken to the nearest public university hospital, which is able to administer 24/7 primary percutaneous coronary intervention (PCI) within 60 minutes after a patient with a heart attack arrives at the hospital. Mr. Öztürk is assessed in the emergency department and transferred to the cardiology unit for coronary angiography and PCI in two coronary arteries and a stent in one.

His recovery is uncomplicated, and the results demonstrated on echocardiography are not considered worrisome. Mr. Öztürk is discharged from the hospital after 2 days and is referred to a cardiac rehabilitation program at the hospital.

His hospital costs and the three new medications that he receives on discharge — an anticoagulant, a beta-blocker, and a statin — are covered fully by the Social Security Institution. He makes an appointment the following week to see his family physician and to receive a repeat prescription for the medicines, for which he pays 20% of the cost. He is seen in the university hospital outpatient clinic 6 weeks after his discharge, for which he incurs a small cost.

active purchasing by the Social Security Institution drove efficiency gains by establishing tariffs for paying hospitals, reducing the average length of stay from 5.8 days in 2002 to 4.1 in 2010, and improving occupancy from 59.4% in 2002 to 65.6% in 2011.[5]

Utilization of maternal and child health services and child mortality improved significantly between 2003 and 2008, especially among rural and socioeconomically disadvantaged populations. Meanwhile, provision of free health care services for costly interventions and reduced cost sharing lowered out-of-pocket and catastrophic expenditures. And satisfaction with health services grew from 39.5% in 2003 to 75.9% in 2011.[4]

Several factors contributed to

DENZEL WASHINGTON

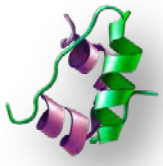
Give a father
no options
and you leave him
no choice.

JOHN Q.

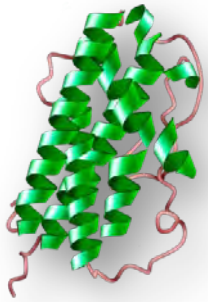
# Generics and Biosimilars

# Biosimilar drugs: concern versus opportunity

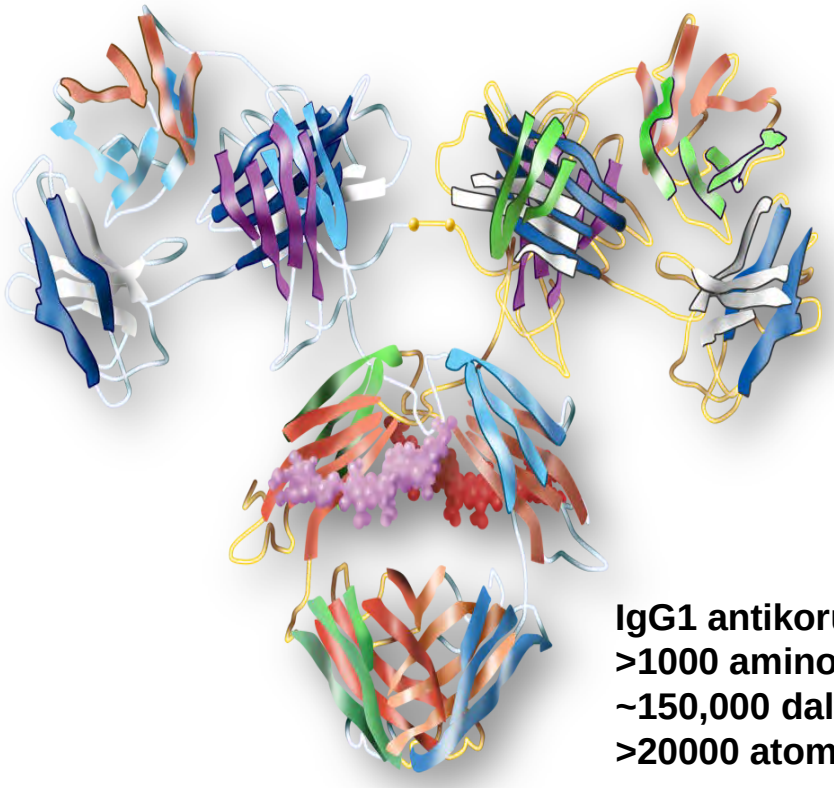
**Aspirin**
**~180 dalton**
**21 atom**



**Insulin**
**51 amino-asit**
**~5,800 dalton**
**788 atom**



**Somatropin**
**191 amino-asit**
**~22,000 dalton**
**3091 atom**



**IgG1 antikoru**
**>1000 amino-asit**
**~150,000 dalton**
**>20000 atom**

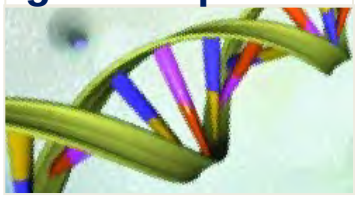
*Genazzazi, AA et. al. (2007) Biosimilar Drugs: Concerns and Opportunities. Biodrugs 2007; 21 (6) :351-356*

# Typical Protein Production Process

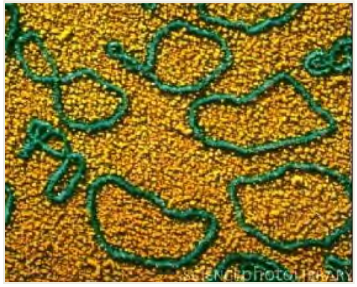
*Different manufacturers will have different processes*

START

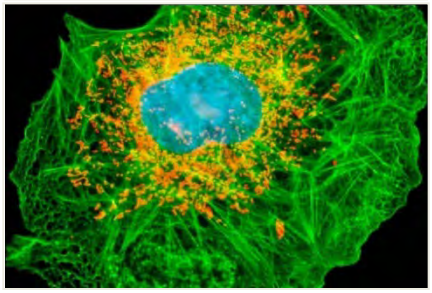
Probably same gene sequence



Different vector



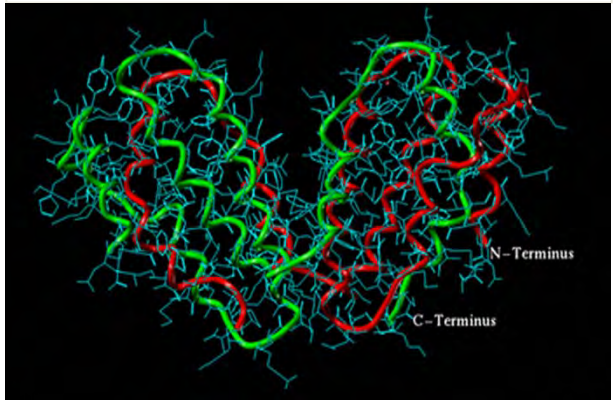
Different host cell



Different fermentation/culture conditions

Different downstream processing

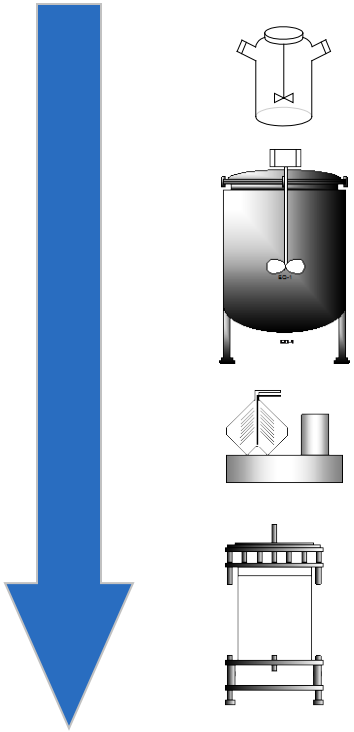
Will result in different biophysical characteristics




END

*KA Burke (2010) Montreal Forum Pharmaceutical Discussions*

# Manufacturing steps may be similar, but will not be identical between different manufacturers



**Purified bulk drug**

| Unit operation | Unique to each manufacturer |
|---|---|
| Cell expansion | Cell line, growth media, method of expansion |
| Cell production in bioreactors | Cell line, growth media, bioreactor conditions |
| Recover through filtration or centrifugation | Operating conditions |
| Purification through chromatography | Binding and elution conditions |
| Characterisation and stability | Methods, reagents, reference standards |

[1]Sharma BG. *EJHP Practice.* 2007;13:54-56; [2]Mellstedt H, et al. *Ann Oncol.* 2008;19:411-419; [3]Roger SD. *Nephrology.* 2006;11:341-346; [4]Power DA, et al. *J Pharm Pract Res.* 2008;38:137-139.

# Evaluation of Biosimilar drugs

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

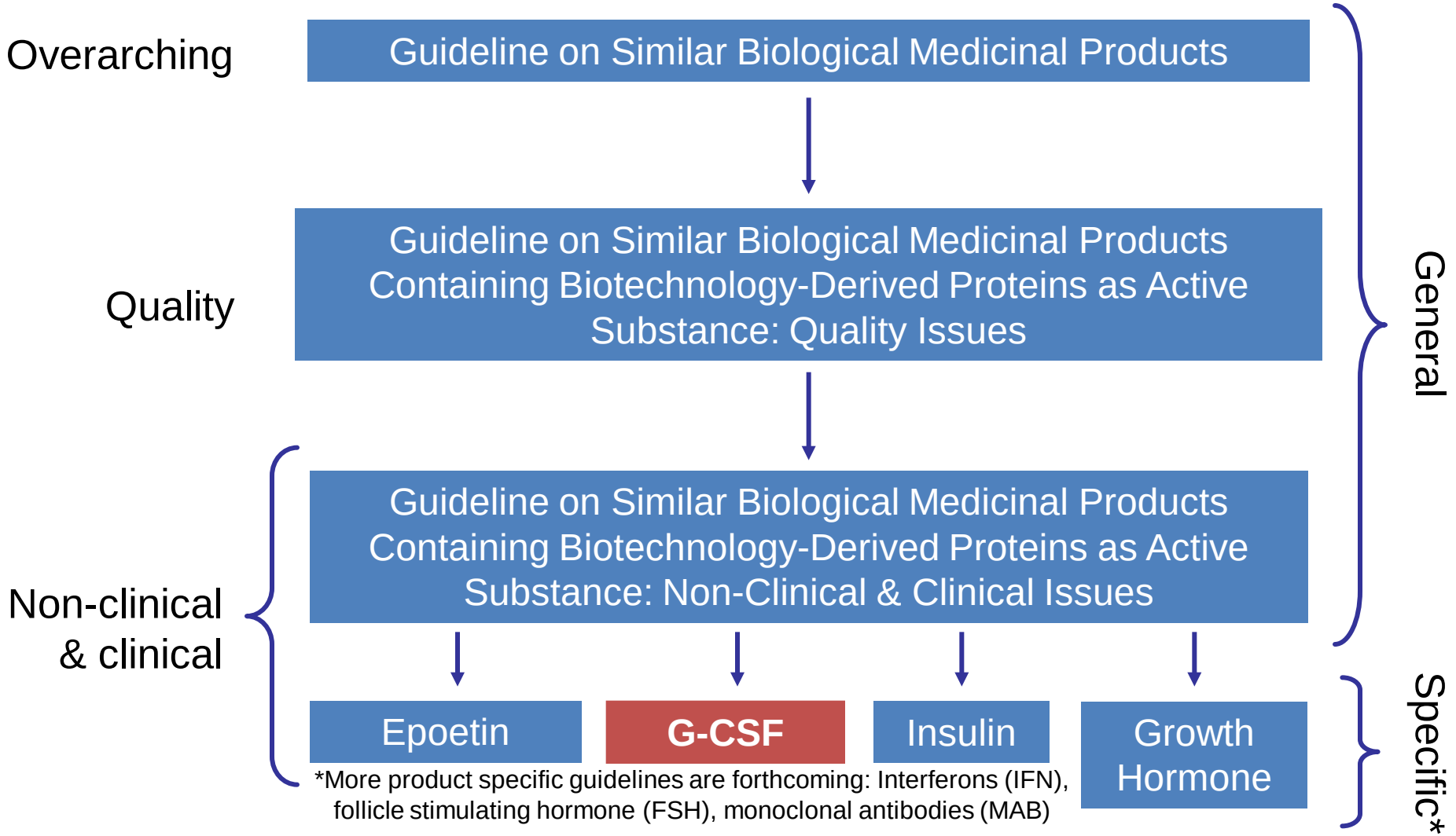
FDA
U.S. Department of Health and Human Services
Food and Drug Administration

Türkiye İlaç ve Tıbbi Cihaz Kurumu
T.C. Sağlık Bakanlığı

**«Farmasötik müstahzarların biyoyararlanım ve biyoeşdeğerliğinin değerlendirilmesi hakkında yönetmelik»**

**27 mayıs 1994**

# European Medicines Agency
# Regulatory Guidelines for Biosimilars




EMA Guideline CHMP/437/04; EMA Guideline EMA/CHMP/BWP/49348/2005; EMA Guideline EMA/CHMP/BMWP/42832/2005; all available at: www.ema.europa.eu

# “..is not the same..” !
# “..nevertheless similar enough..” !
# “..safety and effectiveness..” !

U.S. Food and Drug Administration

U.S. Department of Health and Human Services

FDA Home Page | Search FDA Site | FDA A-Z Index | Contact FDA

**Statement of**

Janet Woodcock, M.D.
Deputy Commissioner, Chief Medical Officer,
Food and Drug Administration

**before**

Subcommittee on Health,
Committee on Energy and Commerce

**“Assessing the Impact of a Safe and Equitable Biosimilar Policy in the United States”**

**May 2, 2007**

**Introduction**

Mr. Chairman and Members of the Subcommittee, I am Janet Woodcock, M.D., Deputy Commissioner, Chief Medical Officer at the U.S. Food and Drug Administration (FDA or the Agency). Thank you for the opportunity to testify about the scientific and regulatory background surrounding follow-on protein products.

During the past several years, there has been increasing public interest in the development of follow-on versions of approved protein products. This interest has been fostered, in part, by advances in manufacturing technology, process control, and characterization that allow greater control over, and understanding about, the physical structure of certain of these products.

However, a number of important issues related to development of such follow-on products also have been identified. First, there is general recognition that the idea of *sameness*, as the term is used in the generic drug approval process under the Federal Food, Drug, and Cosmetic (FD&C) Act and applied to small molecules, will not usually be appropriate for more structurally complex molecules of the type generally licensed as biological products under the Public Health Service (PHS) Act. Additionally, as a related matter, there are clearly scientific challenges involved in determining that a molecule that is not the same as an approved or licensed version is nevertheless similar enough that the Agency’s conclusions about the safety and effectiveness of the approved or licensed version could be relied on to support approval of the follow-on product.

http://www.fda.gov/ola/2007/policy05022007.html

# BİYOBENZER TIBBİ ÜRÜNLERE İLİŞKİN KILAVUZ

İlaç ve Eczacılık Genel Müdürlüğü

| | Klasik Eşdeğer Ürün | Biyobenzer Ürün | Yeni Ürün (Tam Dosya) |
|---|---|---|---|
| Kalite | "Tam ve Bağımsız Ürünün dosya bilgileri " Referans ürünle karşılaştırması | "Tam ve Bağımsız Ürünün dosya bilgileri" Referans ürünle kapsamlı olarak karşılaştırılması | Tam ve Bağımsız ürünün dosya bilgileri |
| Klinik Öncesi | ----- | Kısaltılmış program, molekülün karmaşıklığına bağlı olarak subkronik toksisite çalışması (4 hafta), Lokal tolerans, PK/PD çalışması (farmakokinetik/farmakodinamik) | Klinik Öncesi Tam çalışma |
| Klinik | Bioeşdeğerlilik çalışması | Faz 1:PK/PD çalışması (farmakokinetik/farmakodinamik)<br><br>Faz II çalışması gerekmemektedir<br><br>Gerektiğinde her bir endikasyonda faz III çalışması<br><br>Risk Yönetim Planı | Faz 1<br><br>Faz II<br><br>Tüm endikasyonlarda faz III çalışması<br><br>Risk Yönetim Planı |

| Production step | Conventional generics | Biosimilars |
|---|---|---|
| **Manufacturing** | **Chemical synthesis<br>Simple microbial fermentation<br>Standard analytical methodology** | **Genetically modified cell lines<br>Complex fermentation and purification processes<br>Formulation<br>Complex analytical characterization** |
| **Preclinic** | **Generally none** | **In vitro/in vivo bioassay<br>Toxicity studies<br>Local tolerance studies<br>PK/PD studies** |
| **Clinic** | **Generally BE study** | **Phase I PK/PD<br>Phase III studies<br>Phase IIIb studies<br>Phase IV studies (PMS)** |

*P Saenger (2009) Int J Ped Endocrinol*

# Regulation

Generics and biosimilar medicinal products are regulated in Turkey according to

- Regulation on the Registration of Medicinal Products for Human Use [1]
- Biosimilar Medicinal Products Guideline [2]

1. Official Gazette #25705 of 19.01.2005
2. Ministry Approval No:5285, Date: 07.08.2008

# Biosimilars

- Active substance of the biosimilar should show molecular and biological similarity to the active substance of the reference medicinal product.
- Should be similar to licensed biological reference product in terms of efficacy, safety and quality.
- Comparability studies with reference biological product are required
- The pharmaceutical form, strength and route of administration of the biosimilar should be same with the reference biological product

# Reference Biological Product

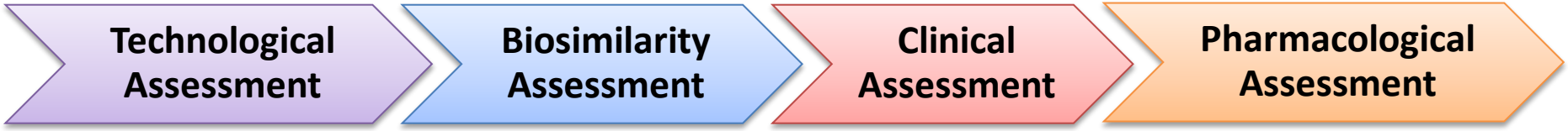
- Reference (original) biological product chosen for comparability testing does not need to be particularly approved in Turkey

- Any difference between biosimilar medicinal product and the reference requires additional evaluation with appropriate studies to ensure efficacy, safety and quality

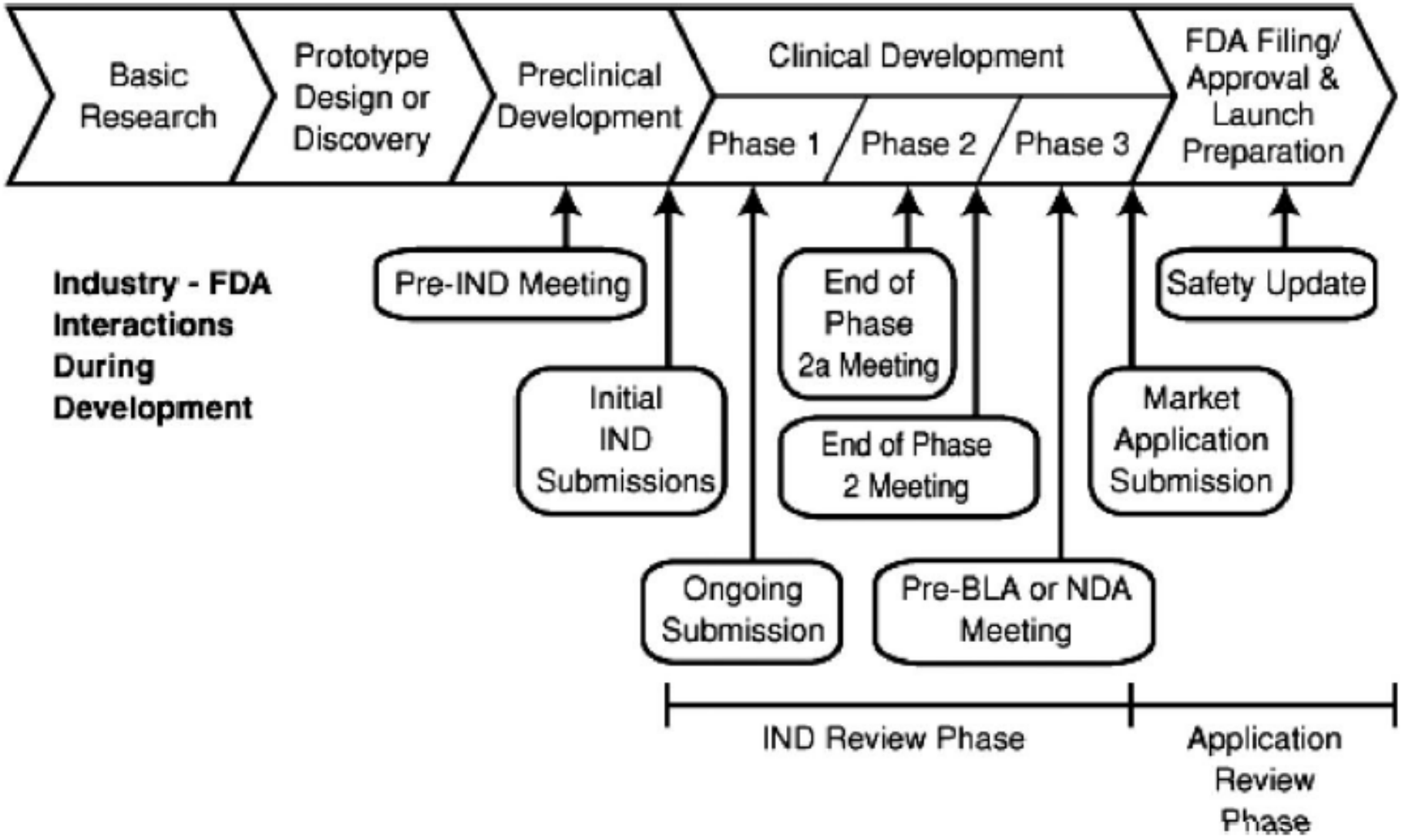
# Approval Track of Generics and Biosimilars

- Generics


- Biosimilars




CLINICAL TRIALS FOR BIOSIMILARS


Basic Research
Prototype Design or Discovery
Preclinical Development
Clinical Development
Phase 1
Phase 2
Phase 3
FDA Filing/ Approval & Launch Preparation
Industry - FDA Interactions During Development
Pre-IND Meeting
Initial IND Submissions
Ongoing Submission
End of Phase 2a Meeting
End of Phase 2 Meeting
Pre-BLA or NDA Meeting
Market Application Submission
Safety Update
IND Review Phase
Application Review Phase

# Phase 4 research: what happens when the rubber meets the road?

*Mark Crowther*[1]

[1]*Division of Hematology and Thromboembolism, St Joseph's Hospital, Hamilton, ON*

A Fresh Look at Drug Approval: Moving Away from Tradition

# Drug discovery in rare indications: opportunities and challenges

*Victoria M. Richon*[1]

A Fresh Look at Drug Approval: Moving Away from Tradition

# Accelerating safe drug development: an ideal approach to approval

*Michael R. Grever*[1]

[1]*Division of Hematology, Ohio State University Medical Center, Columbus, OH*

# The "academic cartel": another pernicious weed in the field of academic medicine

In his timely editorial,[1] Dr Kaushansky articulates his concerns about the various forms of research misconduct that, as he pointed out, are certainly on the increase. He considers certain types of misconduct pernicious. I would like to bring attention to another form of misconduct that has not received much attention in the scientific arena but that is, nevertheless, a pernicious development: the "academic cartel." This is analogous to the industrial, financial, and drug cartels that use devious techniques to promote their products and to sabotage or destroy their opponents. A handful of academics and institutions decide that a particular subject or area of research is "their domain" and make conscious and conceited efforts to propagate and promote their points of view while dismissing or suppressing any differing views. They assume a self-appointed "expert" role in the area of their interest to disseminate their views. Unfortunately, these alleged experts are very often asked to referee scientific work generated by others working in their domain. Consequently, the articles supporting their point of view are accepted and published often with fantastic proclamations ("breakthrough," "revolutionary," "cutting edge," etc) while suppressing works that differ from or challenge their views. In my opinion, this is pernicious and deleterious to scientific and medical research in general, especially if the subject matter has an important public health (for example, blood transfusion medicine) or clinical implication. I think it is the responsibility of the editors of various high-impact journals, which I think includes *Blood,* to be aware of this practice and to choose appropriate referees to review articles submitted. I also think that editors should be made accountable if they fail to curb this practice of prejudiced publication.

**Muttuswamy Sivakumaran**

*Correspondence: Department of Haematology, Peterborough District Hospital, Thorpe Road, Peterborough, PE3 6DA, United Kingdom; e-mail: muttuswamy.sivakumaran@pbh-tr.anglox.nhs.uk*

## Reference

1. Kaushansky K. Removing the cloud from industry-sponsored, multicentred clinical trials. Blood. 2001;98:2001.

# Removing the cloud from industry-sponsored, multicentered clinical trials

While sitting in a scientific meeting several years ago, I noted that the slides for 3 consecutive reports of clinical trials of a new therapeutic agent, presented by investigators from 3 separate academic institutions, utilized precisely the same format, font, color scheme, and computer graphics program. Afterward I found out that this was not coincidence; the pharmaceutical company sponsoring the trials had taken the raw data from the investigators, analyzed it, and then provided the slides for presentation. Many of

> numerous occasions, the lead author has not written the paper bearing his/her name; ghostwriters working for the pharmaceutical company sponsoring the trial have actually penned much of the manuscript based on the company's internal analysis of the primary data collected from the clinical investigators at participating academic medical centers. How has such a system of ghost-analysis and ghostwriting in multicentered therapeutic clinical trials come into being? This is apparently the way some in the pharmaceutical industry design their studies, a process enforced by the threat of withdrawal of future financial support for clinical trials. Unfortunately, there are many well-known examples of gross

**Kenneth Kaushansky**
*Editor-in-Chief*
*Seattle, WA*

# Approved Biosimilars in Turkey

| Product Name | Active Substance | Production Site | Year of approval |
|---|---|---|---|
| Dropoetin (3)* | Epoetin alpha | Turkey | 2013 |
| Enox (5) | Enoxaparin sodium | Turkey | 2013 |
| Epoplus | Epoetin alpha | Cuba | 2013 |
| Clotinab | Abciximab | South Korea | 2012 |
| Oksapar (6) | Enoxaparin sodium | Turkey | 2012-2013** |
| Eporon (3) | Epoetin alpha | South Korea | 2011 |
| Omnitrope (2) | Somatropin | Austria | 2011 |
| Epobel (8) | Epoetin zeta | Germany | 2009 |
| Leucostim (2) | Filgrastim | South Korea | 2009 |

*Numbers next to product names represent the available different strenghts for each product
** 4 different strenghts of Oksapar approved in 2012 and 2 strengths approved in 2013

**Courtesy of Adem Abay, Turkish Medicines and Medical Devices Agency**

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2 of 3

**Biosimilar filgrastim (Leucostim (R)) seems to have similar efficacy in hematopoietic progenitor cell mobilization compared to original filgrastim (Neupogen (R)) and lenograstim (Granocyte (R)): a retrospective, multicenter analysis**

By: Tekgunduz, AIE (Tekgunduz, A. I. E.)[1]; Kaya, AH (Kaya, A. H.)[1]; Goker, H (Goker, H.)[2]; Ozdemir, E (Ozdemir, E.)[3]; Iskender, D (Iskender, D.)[1]; Kocubaba, S (Kocubaba, S.)[1]; Koyikci, O (Koyikci, O.)[1]; Altuntas, F (Altuntas, F.)[1]

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**The comparison of Filgrastim (Neupogen (R)), Lenograstim (Granocyte (R)) as a first line pe autologous hematopoieitic stem cell transplar**

By: Sivgin, S (Sivgin, Serdar)[1]; Karakus, E (Karakus, Esen)[1]; Kaynar Cigdem)[1]; Keklik, M (Keklik, Muzaffer)[1]; Zararsiz, G (Zararsiz, Gokm (Cetin, Mustafa)[1] ...More

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TRANSFUSION AND APHERESIS SCIENCE
**Volume:** 48 **Issue:** 3 **Pages:** 315-320
**DOI:** 10.1016/j.transci.2013.04.007
**Published:** JUN 2013
View Journal Information

**Abstract**

Objectives and aim: Patients affected by hematological malignancies can c cells (PBSCs) transplantation. Different strategies have been used to mobil factor (G-CSF) alone or chemotherapy plus G-CSF. In this study, we aimec (Neupogen (R)), biosimilar filgrastim (Leucostim (R)) and Lenograstim (Grar hematopoietic stem cell transplantation (autoHSCT).

Materials and methods: We retrospectively analysed data of patients who Lymphoma (HL), non-Hodgkin Lymphoma (NHL) and others. Data for stem Filgrastim (Neupogen (R)), biosimilar Filgrastim (Leucostim (R), Group) and count at the end of mobilization procedure.

Results: A total of 96 patients who underwent autoHSCF were retrospective male. The diagnosis of the patients were; multiple myeloma (39 patients, 4 patients, 16.6%), and others (18 patients, 18.9%). The median number of CD34(+)/kg was 2 in Neupogen (R) (min-max: 1-4) and Granocyte (R) (min-

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# The comparison of Filgrastim (Neupogen®), biosimilar filgrastim (Leucostim®) and Lenograstim (Granocyte®) as a first line peripheral blood stem cell mobilization strategy in autologous hematopoieitic stem cell transplantation: A single center experience from Turkey

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ARTICLE INFO

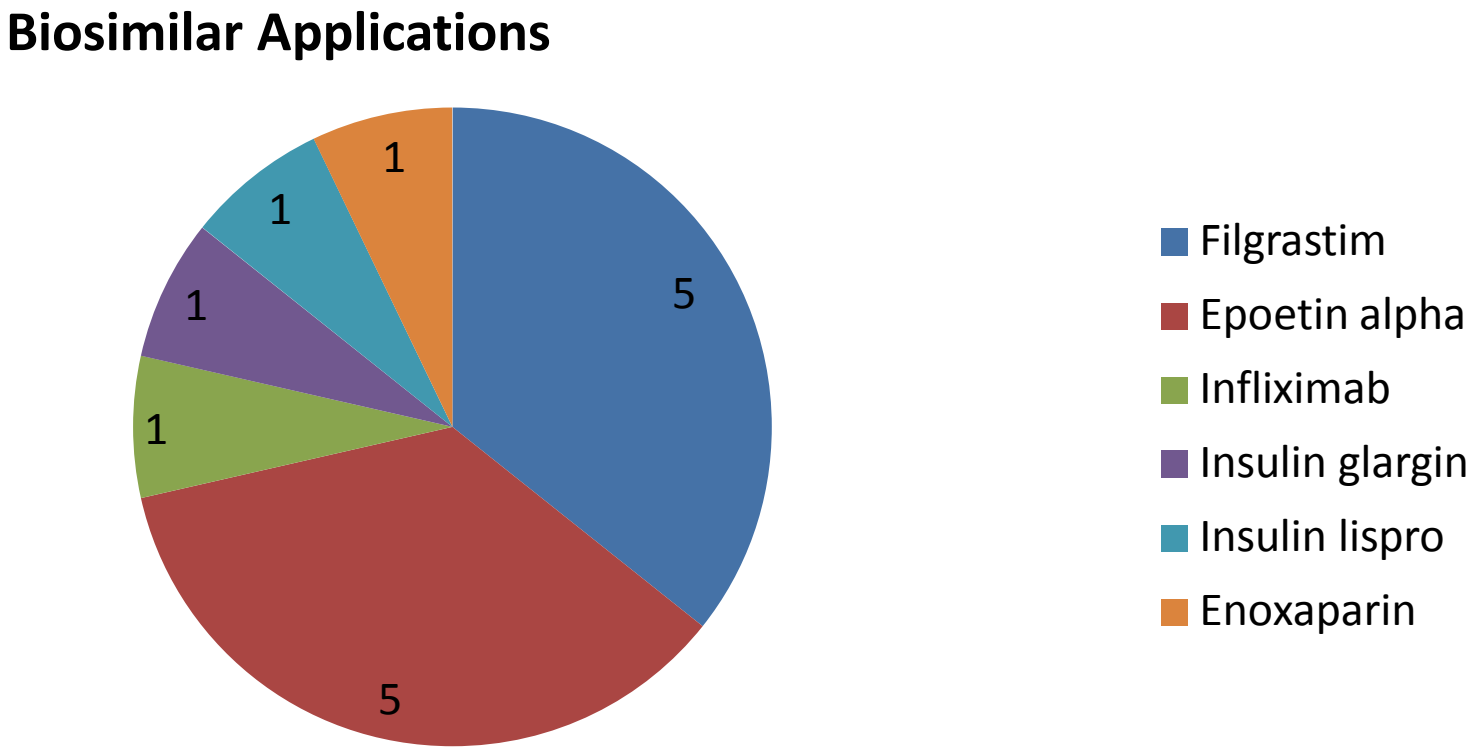
*Keywords:*
Autologous hematopoietic stem cell transplantation
Stem cell mobilization
G-CSF

ABSTRACT

*Objectives and aim:* Patients affected by hematological malignancies can often benefit from high dose chemotherapy followed by peripheral blood stem cells (PBSCs) transplantation. Different strategies have been used to mobilize an adequate number of PBSC, including granulocyte colony-stimulating factor (G-CSF) alone or chemotherapy plus G-CSF. In this study, we aimed to compare the efficacy profile of different G-CSF agents including filgra-

# Biosimilar Products on the List

- Application procedures continue for 14 biosimilar products

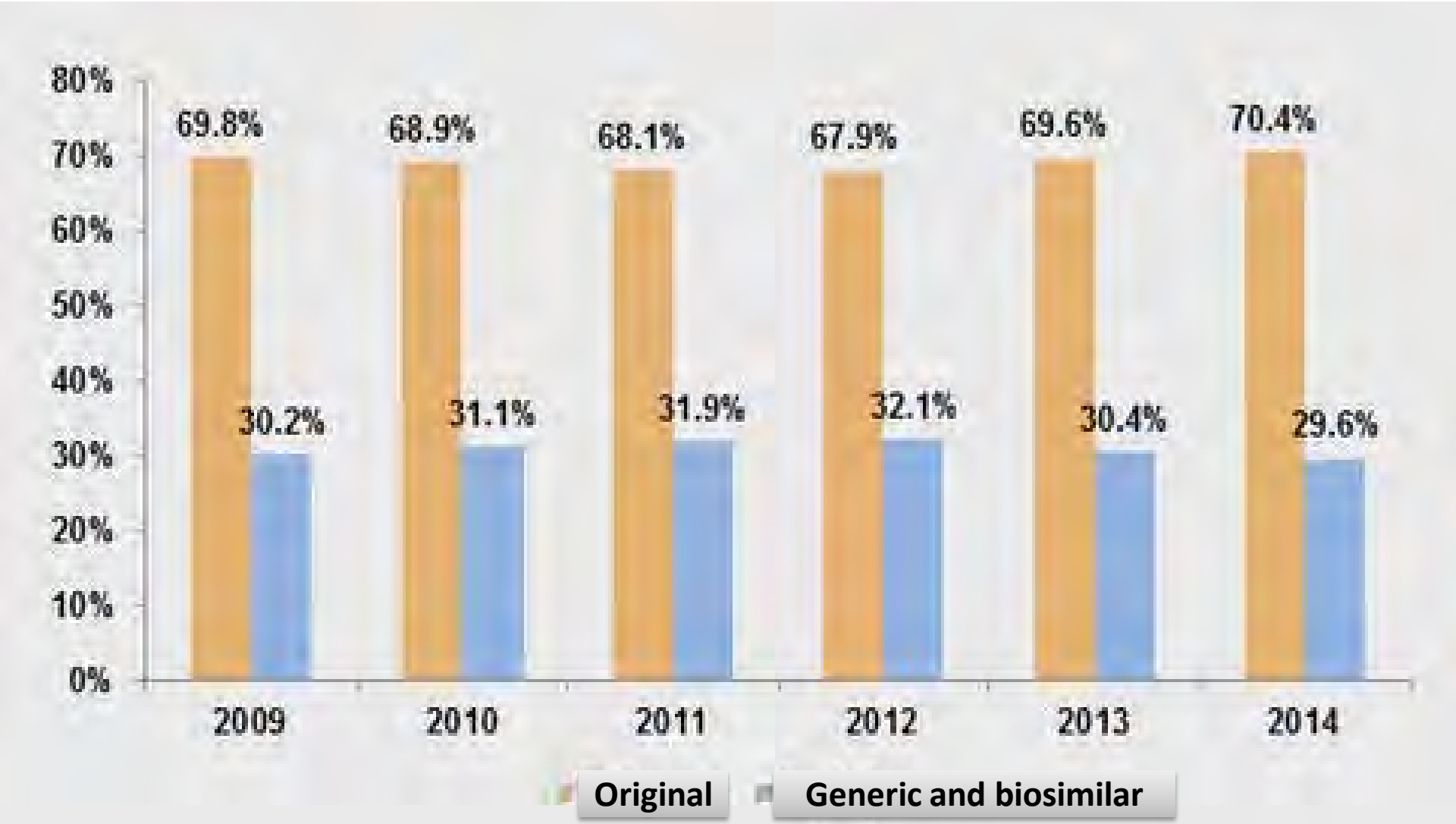



Courtesy of Adem Abay, Turkish Medicines and Medical Devices Agency

# Drug Market Size of Turkey

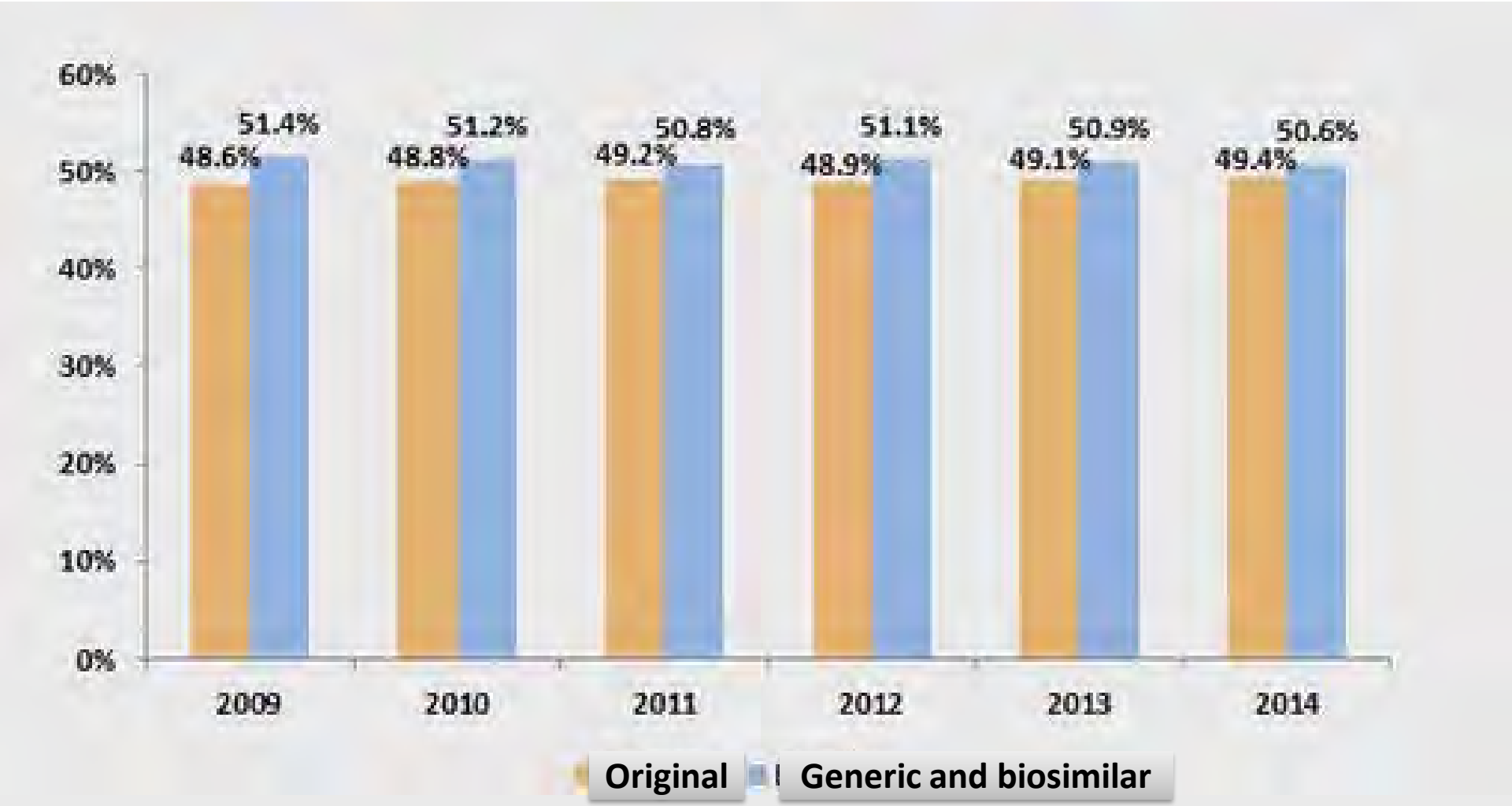

Source: IMS Health

# Drug Expenses (TRL)



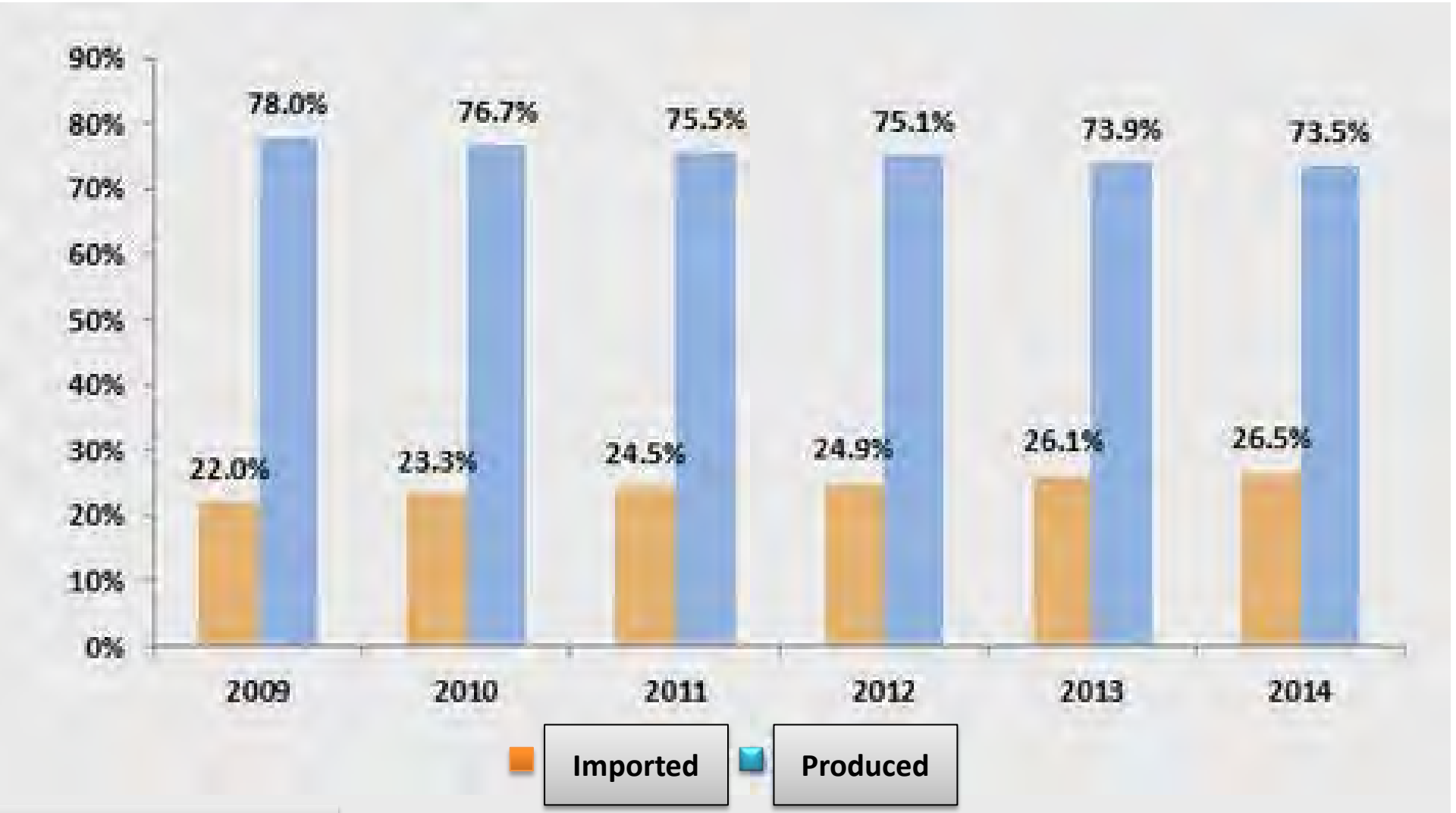

Source: IMS Health

# Market Share (Units)



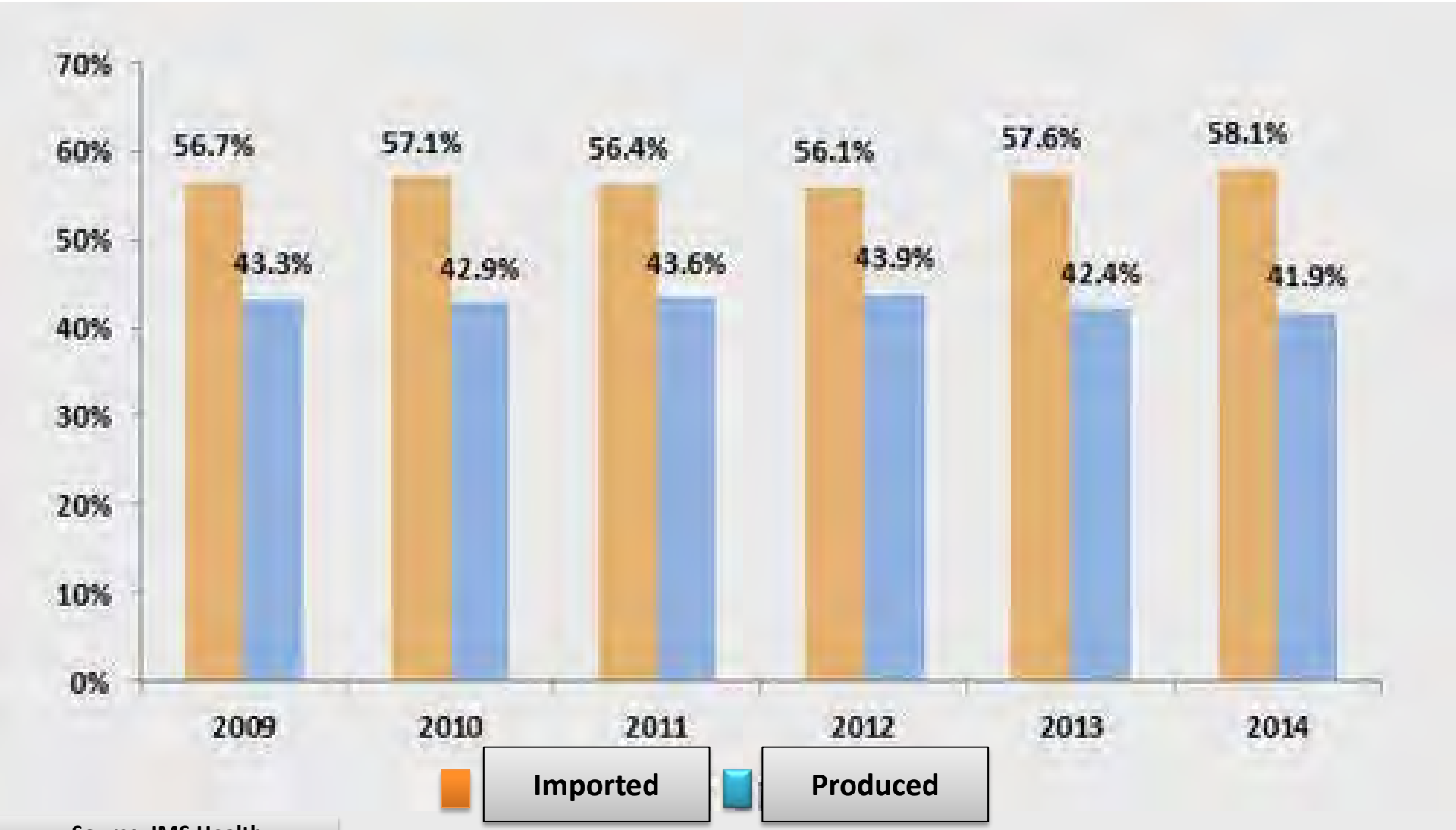

Source: IMS Health

# Market Share (Units)




Source: IMS Health

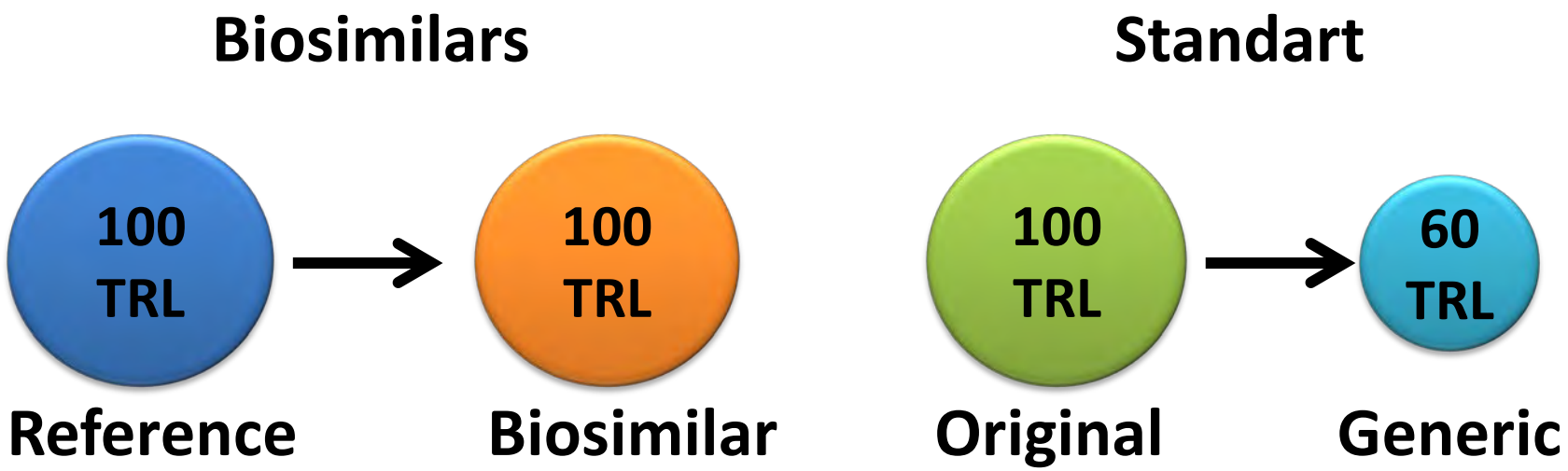
# Market Share (TRL)




Source: IMS Health

# Pricing of Generics and Biosimilars

- Notification on the pricing of medicinal products for human use:*




*Official Gazette #26651/22.09.2007 amended by OG-14/4/2012-28264

**Courtesy of Adem Abay, Turkish Medicines and Medical Devices Agency**

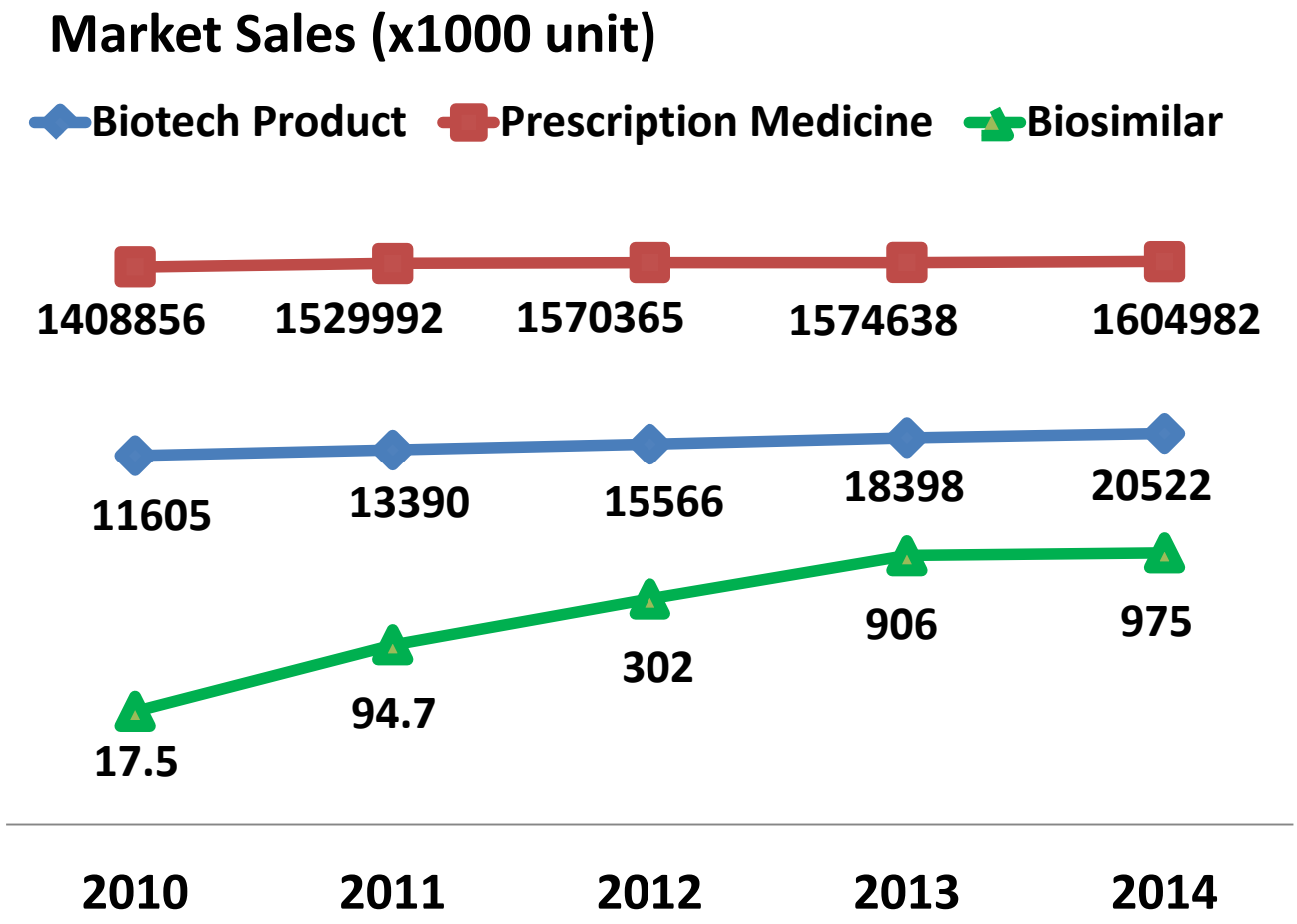
# Incentives for Biosimilars

- Decision of the Council of Ministers on Promoting Investments:[1]
  - Investments above 20 million TRL for biotechnological products (including biosimilars), oncology drugs and blood products will be prioritised and supported

- Ministry of Health / The Scientific and Technological Research Council of Turkey (TÜBİTAK) has issued a project call for the *'Development and production of biosimilars in Turkey'*.[2]

1. **Decision No: 2012/3305, Date: 19.06.2012**
2. **1007 Program call from TÜBİTAK announced at 05.08.2013 and closed at 08.11.2013**

# Biosimilars on Turkish Drug Market




| Change 2013/2014 | |
|---|---|
| Unit | Value (TRL) |
| 1.9% | 8% |
| 11.5% | 20.5% |
| 7.5% | 26.8% |

Source: IMS Health 2014

# Medium Term Development Plan

- Plasma fractination plant to produce plasma derived blood products
- Co-operation with biotech companies to produce recombinant coagulation factors
- Vaccine production
- Insulin production

# Conclusion

- Generics and biosimilars are of top priority…
- Number of applications for biosimilar drugs is expected to increase
- Well-defined, class/product specific guidelines and regulations will secure quality, efficacy and safety of both generics and biosimilars

# The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts

Experts in Chronic Myeloid Leukemia

**As a group of more than 100 experts in chronic myeloid leukemia (CML), we draw attention to the high prices of cancer drugs, with the particular focus on the prices of approved tyrosine kinase inhibitors for the treatment of CML. This editorial addresses the multiple factors involved in cancer drug pricing and their impact on individual patients and health care policies, and argues for the need to (1) lower the prices of cancer drugs to allow more patients to afford them and (2) maintain sound long-term health care policies. (*Blood*. 2013;121(22):4439-4442)**



John Goldman; Ibrahim Haznedaroglu; Henrik Hjorth-Hansen; Tessa Holyoake; Brian Huntly; Philipp le Coutre; Elza Lomaia; Francois-Xavier Mahon; David Marin-Costa; Giovanni Martinelli; Jiri Mayer; Dragana Milojkovic; Eduardo Olavarria; Kimmo Porkka; Johan Richter; Philippe Rousselot; Giuseppe Saglio; Guray Saydam; Jesper Stentoft; Anna Turkina; Paolo Vigneri; Andrey Zaritskey.

**Latin America**

Alvaro Aguayo; Manuel Ayala; Israel Bendit; Raquel Maria Bengio; Carlos Best; Eduardo Bullorsky; Eduardo Cervera; Carmino DeSouza; Ernesto Fanilla; David Gomez-Almaguer; Nelson Hamerschlak; Jose Lopez; Alicia Magarinos; Luis Meillon; Jorge Milone; Beatriz Moiraghi; Ricardo Pasquini; Carolina Pavlovsky; Guillermo J. Ruiz-Arguelles; Nelson Spector.

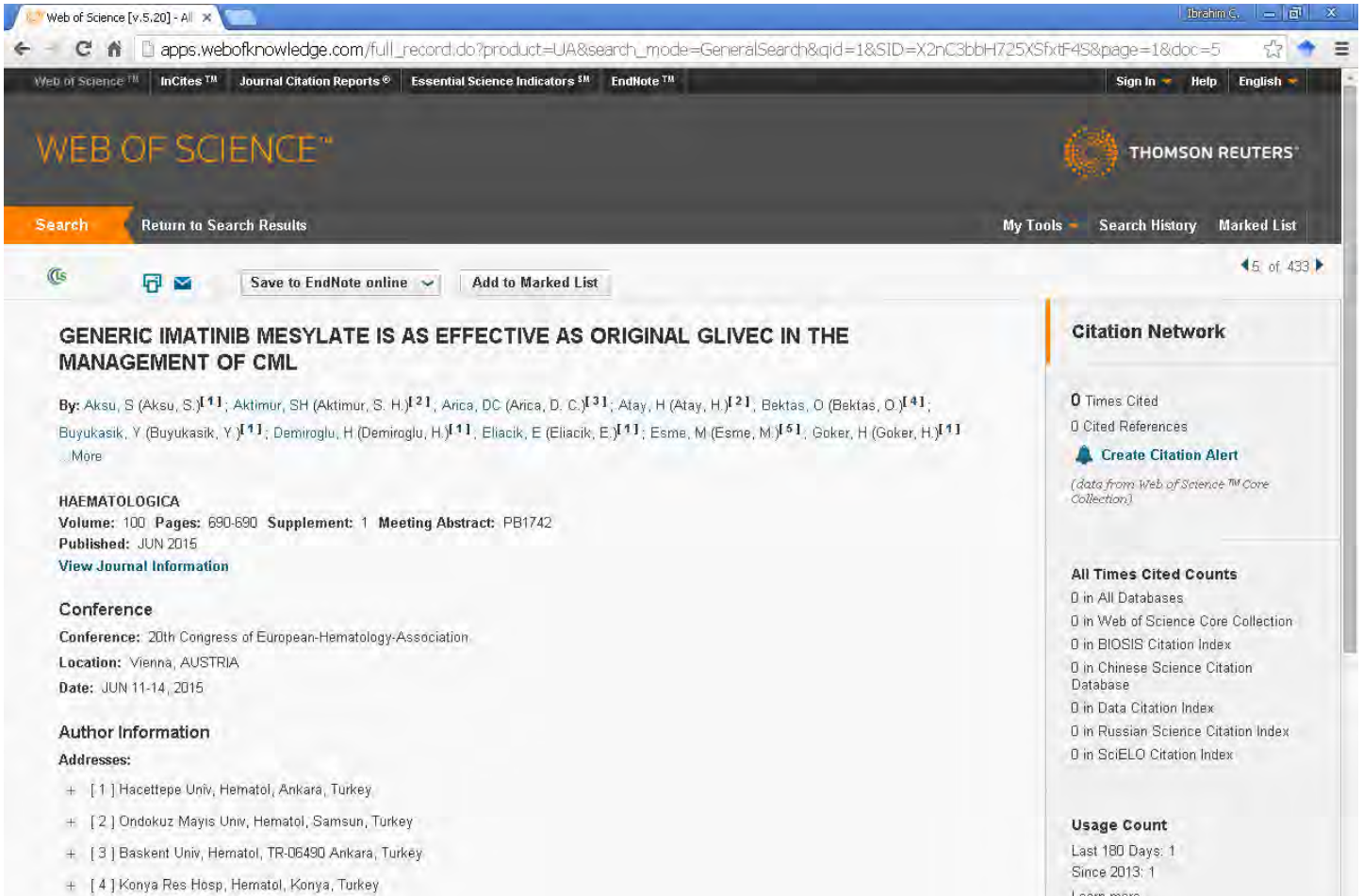
**Australia and Asia**

Christopher Arthur; Peter Browett; Andrew Grigg; Jianda Hu; Xiao-jun Huang; Tim Hughes; Qian Jiang; Saengsuree Jootar; Dong-Wook Kim; Hemant Malhotra; Pankaj Malhotra; Itaru Matsumura; Junia Melo; Kazunori Ohnishi; Ryuzo Ohno; Tapan Saikia; Anthony P. Schwarer; Naoto Takahashi; Constantine Tam; Tetsuzo Tauchi; Kensuke Usuki; Jianxiang Wang.

**Middle East and Africa**

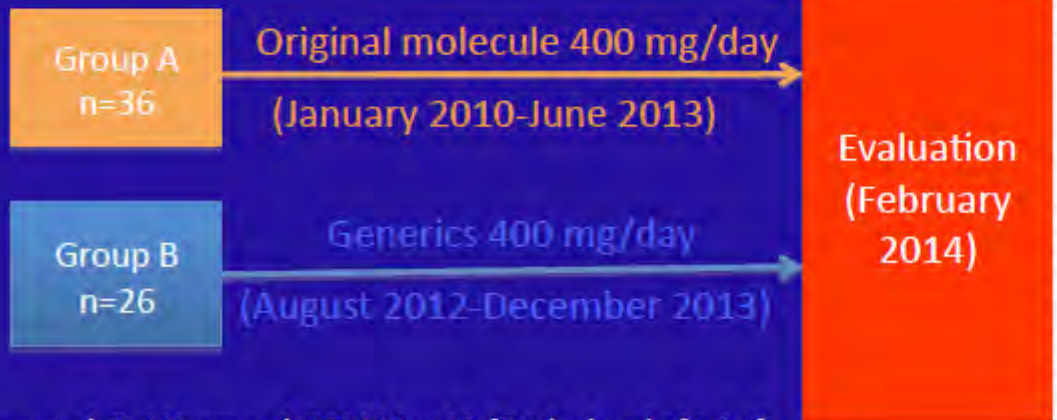
Fawzi Abdel-Rahman; Mahmoud Deeb Saeed Aljurf; Ali Bazarbachi; Dina Ben Yehuda; Naeem Chaudhri; Muheez Durosinmi; Hossam Kamel; Vernon Louw; Bassam Francis Matti; Arnon Nagler; Pia Raanani; Ziad Salem.

approved. This Forum reflects the views of a large group of CML experts who believe that the current prices of CML drugs (1) are too high, (2) are unsustainable, (3) may compromise access of needy patients to highly effective therapy, and (4) are harmful to the sustainability of our national health care systems. These concerns reflect the spiraling prices of cancer drugs in general. Of the 12 drugs



# First-line use of Generics

- To evaluate the efficacy and tolerability of generic imatinib in the **upfront** setting in CP-CML patients.
- 3 centers were enrolled in the study.
- Two study groups;




| Parameter | Group A ($n$ = 36) | Group B ($n$ = 26) | $P$ value |
|---|---|---|---|
| Median age, years (range) | 38 (18–83) | 45 (17–75) | 0·938 |
| Male/female ($n$) | 25/11 | 17/9 | 0·738 |
| Sokal risk low/ intermediate/high ($n$) | 19/15/2 | 11/8/7 | 0·144 |
| Median follow-up under IM, months (range) | 20 (8–48) | 8·5 (2–18) | **<0·001** |
| Number of patients with CCyR at 6 months, $n$ (%) | 20 (56) | 11 (52) | 0·818 |
| Number of patients with MMR at 6 months, $n$ (%) | 12 (33) | 7 (33) | 1 |
| Number of patients who were switched to 2nd generation TKIs due to resistance, $n$ (%) | 4 (11) | 4 (15) | 0·623 |
| Haematological AEs (all grades), $n$ (%) | 5 (14) | 4 (15) | 0·870 |
| Neutropenia | – | 2 (50) | |
| Thrombocytopenia | 5 (100) | 2 (50) | |
| Non-haematological AEs (all grades), $n$ (%) | 7 (19) | 5 (19) | 0·987 |
| Muscle cramps | 5 (71)* | 3 (60) | |
| Oedema | 1 (14)* | 2 (40) | |
| GI symptoms | 3 (43)* | – | |
| Patients requiring IM dose reduction, $n$ (%) | 5 (14) | 3 (12) | 0·787 |

AE, adverse event; CCyR, complete cytogenetic response; GI, gastrointestinal; IM, imatinib mesylate; MMR, major molecular response; TKI, tyrosine kinase inhibitor.
Bold values indicate Group A patients had a longer median follow-up under IM than patients in Group B ($P < 0·001$).
*There were two patients with more than one AE (one with both GI symptoms and muscle cramps, and the other had oedema and muscle cramps), so the rates of non-haematological AEs in this patient

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# Strategies that Delay or Prevent the Timely Availability of Affordable Generic Drugs in the United States

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Department of Leukemia, MD Anderson Cancer Center, Houston, Texas[1], Rutgers Law School, Camden, New Jersey[2], Weill Cornell Medical Center, New York, New York[3]

## Strategies to Delay the Availability of Affordable Generics is a Global Problem

High cancer drug prices are influenced by the availability of generic cancer drugs in a timely manner. Several strategies have been used to delay the availability of affordable generic drugs into the United States and world markets. These include: reverse payment or pay-for-delay, patent settlements, authorize generics, product hopping, lobbying against cross-border drug importation, buying out the competition, and others. In this Forum, we detail these strategies and how they can be prevented.