

# The INN Programme and the safety of INNs

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World Health  
Organization

# Introduction to INN Programme

*"Some activities undertaken by WHO are largely invisible, quietly protecting the health of every person on this planet, every day. By assigning a single international name to drugs, WHO helps ensure that a prescription filled abroad is what doctor ordered back home."*

*Dr Margaret Chan, Director General - Working for Health: An introduction to the WHO*



# WHO some basic facts

- 193 Member States
- Two governing bodies:
  - World Health Assembly
  - Executive Board
- WHO Secretariat:
  - HQ
  - six Regional Offices
  - WHO Expert Panels  
(e.g. on the International Pharmacopoeia and Pharmaceutical Preparations etc.)
  - Constitution 1946, in force since 7 April 1948 (World Health Day)
- ↑ Article 2 (u) International standards



# The WHO International Nonproprietary Name (INN) Programme

*To provide one single name worldwide for active pharmaceutical substances*

- Initiated in 1950 by resolution WHA3.11
- Operational since 1953
- Based on WHO Constitution
- Insulin human (48)(22)

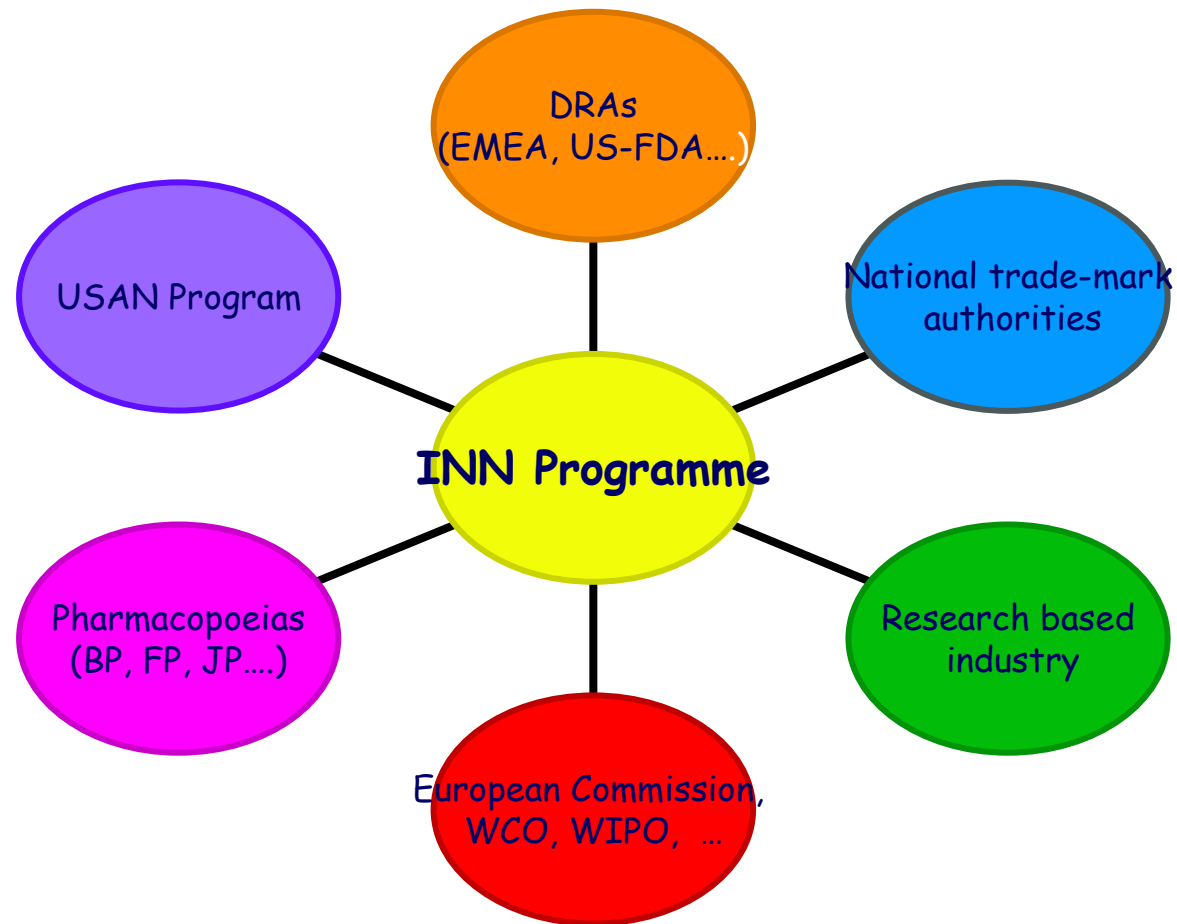


# The WHO International Nonproprietary Name (INN) Programme

- WHO has responsibility to develop, establish and promote international standards for pharmaceutical and biological products
- Need for universally available and accepted name for drug substance
- INN is a unique generic name that is recognized globally and is public property
- Intended for use in drug regulation, prescription, pharmacopoeias, labeling, advertising, scientific literature

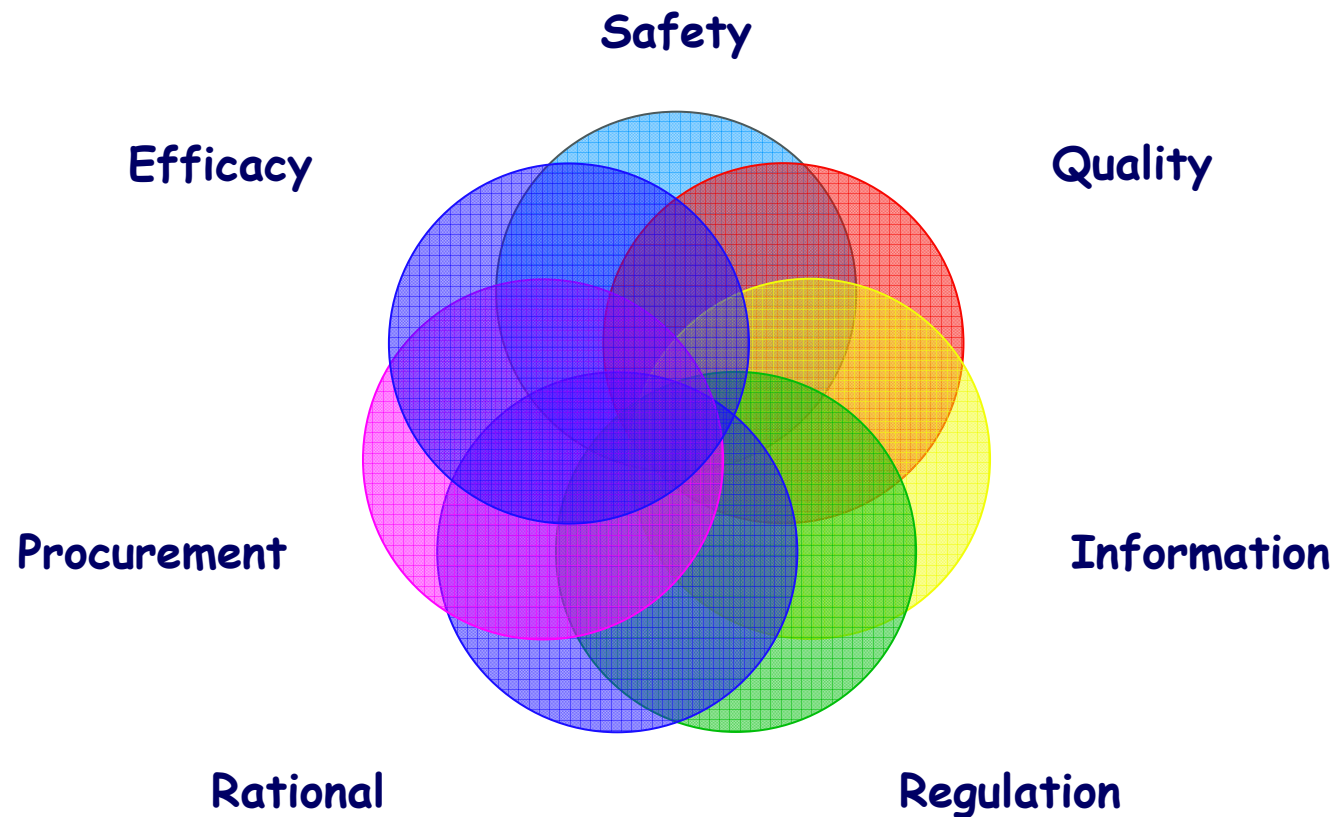


# Interested parties outside WHO



# International Nonproprietary Name (INN) Programme

## What's in a name?



# INNs...

- unique name
- distinctive in sound and spelling
- not liable to confusion with other names in common use
- formally placed by WHO in the public domain, (hence their designation as nonproprietary)
- can be used without any restriction to identify pharmaceutical substances





# The INN System

- WHO Secretariat
- INN Expert Group
  - Can call on further experts if necessary
  - INN Advisory Group on Biologicals
- Publications



# INN selection process

- Secretariat receives INN applications
- Consultation / INN Expert Group
- Secretariat informs applicants
- Validation of Information
- Published in a List of proposed INN
- 4-month period for objections and comments
- Published in a List of recommended INN



# INN Lists

- INN Lists are published in **WHO Drug Information**: 2 proposed and 2 recommended lists every year in English, French, Spanish and Latin.
- All INNs are published in a **cumulative list** with additionally INNs in Arabic, Chinese and Russian.
- About 8500 INNs have been published

<http://www.who.int/medicines/services/inn/publication/en/index.html>.

- On-line INN information: [Mednet - INN Extranet](#)



# INN Cumulative List 14

- **Portable format**

- Information over 8500 published INN (names, structures,...)

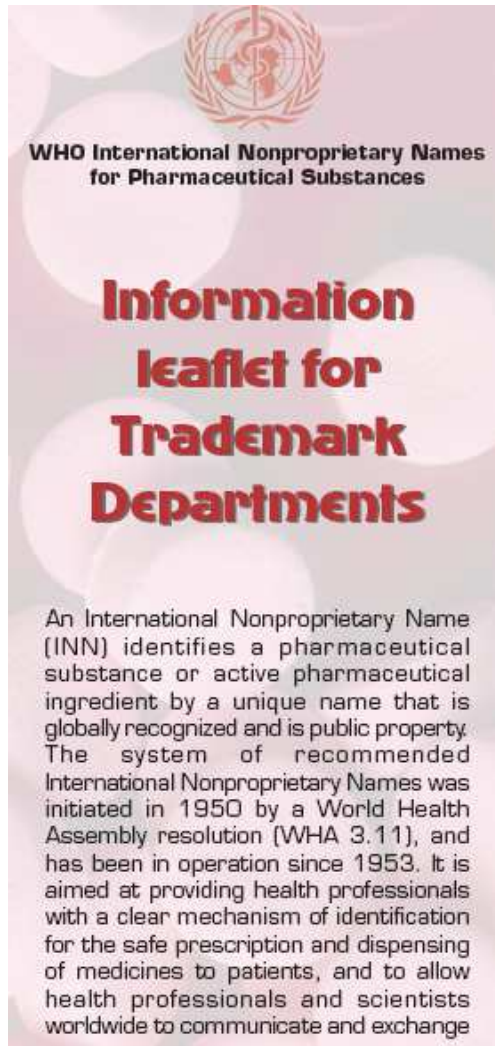
- **Published every two years**

- **Searchable database**

- All or part of name (e.g. *-profen*)
- In the six UN official languages
- CAS RN
- Alternate names
- ATC (Anatomic Therapeutic Chemical) codes
- Etc...



# INN Protection



INNs have to be distinctive in sound and spelling, and should not be liable to confusion with other names in common use....they are formally placed by WHO in the public domain

[INN Leaflet for TM departments.](#)

# Use of stems

## ➤ Names of "pharmacologically-related" substances have a common stem

- To indicate chemical and /or pharmacological group relationship
- Published for 'established series of related compounds'
- WHO publication ' *The use of stems in the selection of INN*'
- INNs and stems have protection within trade mark arena
- Stem book 2011+ Addendum (when necessary)
- pre-stems list

# INN Stem: Marketing exercise ?

- *Latin*                      *English*  
  
-*acum*                      -*ac*                      anti-inflammatory agents, ibufenac derivatives  
  
-*coxibum*                      -*coxib*                      selective cyclo-oxygenase inhibitors .....
- -*pristone*                      -*prisnil*
- *"Guidance on the establishment of new INN stems"*  
(INN Working Doc. 07.215)

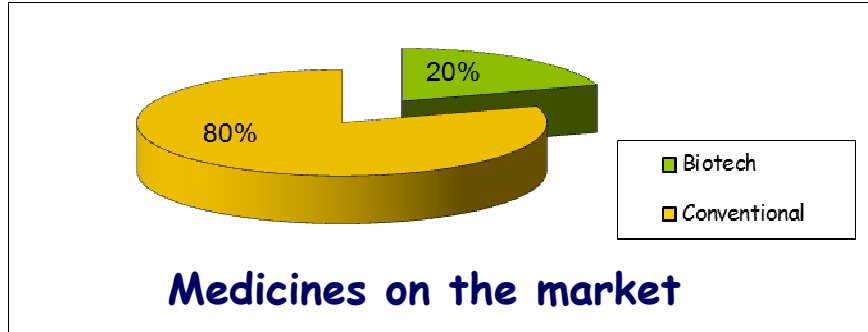
# Challenges

- **Protection of INNs: need to improve collaboration with DRAs (WHA46.19) and INN users.**
- **Userfriendliness of INNs: need to avoid unpronounceable INNs that discourage use of generic names**

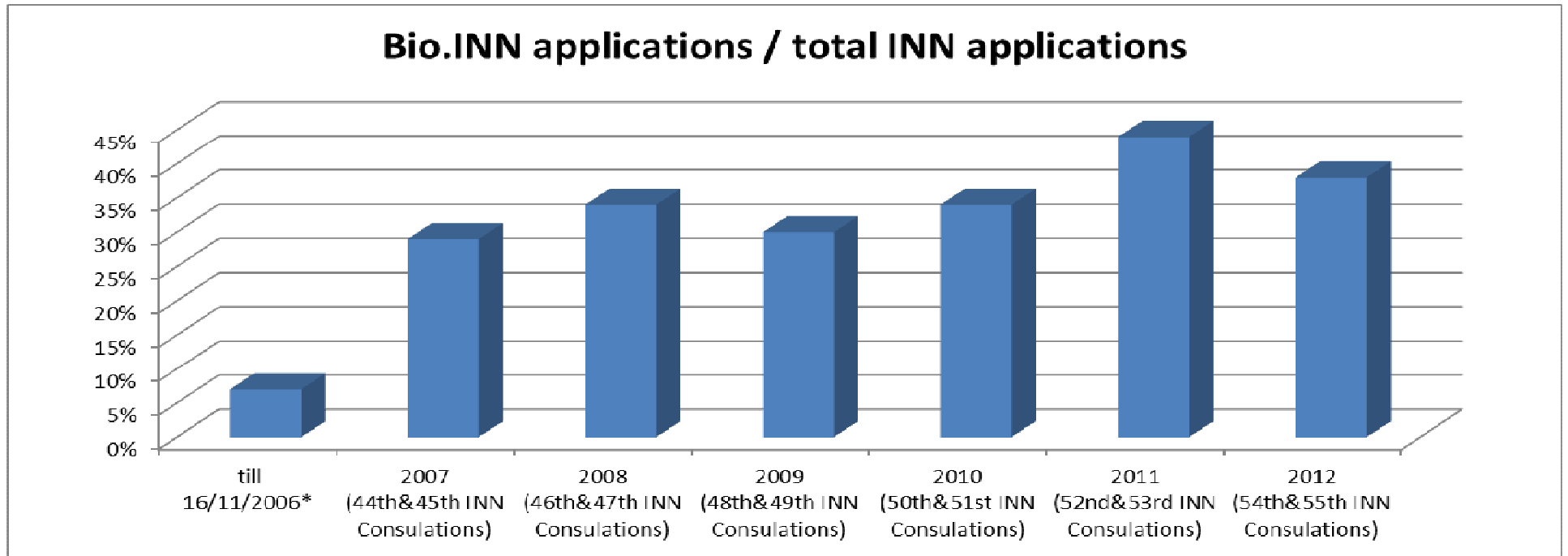
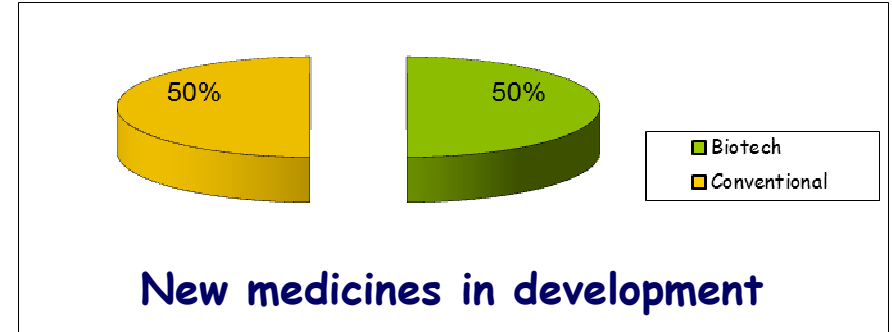




# The number of Bio. INN requests has been increasing



(European Commission 2005)



# General policies

Blood products	natural excluded
Fusion proteins	
Gene therapy products	
Glycosylated proteins/peptides	
Non-glycosylated proteins/peptides	
Immunoglobulins	excluded
Monoclonal antibodies	
Skin substitutes	excluded
Transgenic products	
Vaccines	most excluded
Cell therapy products	under discussion



# Existing INN stems for biological and biotechnological substances

Name of the group	Stem	Name of the group	Stem
antisense oligonucleotides	<i>-rsen</i>	pituitary hormone-release inhibiting peptides	<i>-relix</i>
blood coagulation cascade inhibitors	<i>-cogin</i>	interleukin receptor antagonists	<i>-kinra</i>
blood coagulation factors	<i>-cog</i>	interleukin type substances	<i>-kin</i>
colony stimulating factors	<i>-stim</i>	monoclonal antibodies	<i>-mab</i>
enzymes	<i>-ase</i>	oxytocin derivatives	<i>-tocin</i>
erythropoietin type blood factors	<i>-poetin</i>	peptides and glycopeptides (for special groups of peptides see <i>-actide</i> , <i>-pressin</i> , <i>-relin</i> , <i>-tocin</i> )	<i>-tide</i>
growth factors	<i>-ermin</i>	pituitary hormone-release stimulating peptides	<i>-relin</i>
growth hormone derivatives	<i>som-</i>	receptor molecules, native or modified (a preceding infix should designate the target)	<i>-cept</i>
heparin derivatives including low molecular mass heparins	<i>-parin</i>	synthetic polypeptides with a corticotropin-like action	<i>-actide</i>
hirudin derivatives	<i>-irudin</i>	vasoconstrictors, vasopressin derivatives	<i>-pressin</i>



# Glycosylated proteins/peptides

- Identify the group with a stem (*-poetin*)
- Indicate differences in the amino acid sequence with a random prefix (*darbepoetin alfa*)
- Indicate differences in the glycosylation pattern with a Greek letter in full as second word (*epoetin alfa, beta, gamma, delta, etc*)
- Greek letters assigned in the alphabetical sequence as applications received



# Biosimilars – considerations

- The concept of biosimilar is a regulatory one.
- Generic substitution and reimbursement are health policy matters.
- Decision on interchangeability is not done by WHO.
- INNs are part of the pharmacovigilance system.
- There is no specific INN policy for biosimilars (currently).
- Glycosylated proteins from different sources expected to differ in their glycosylation profile so are given distinct names; the same approach is valid for all the other post-translational modifications.



# Naming of Similar Biotherapeutics Products

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The WHO INN Programme exists to facilitate the identification of medicines so that they:

- have a unique name that is globally recognised; and
- are prescribed and used rationally and safely

At present SBPs are not specifically named, but the general naming principles are applied.



# Current WHO policy

Issue	Generics	SBP Type 1	SBP Type 2	Non-SBP
Quality characteristics	Same	Highly similar & cannot be distinguished from reference by analytical quality testing.	Comparable to reference, but significant differences in analysed parameters.	Not comparable
Amino acid sequence	N/a	Same	Same	Similar to different
Post-translational modification	N/a	Highly similar	Similar to different	Different
Efficacy - safety	Bioequivalent	Comparable	Comparable	Similar to different
<b>INN</b>	<b>Same INN as reference</b>	<b>Same INN as reference</b>	<b>Same INN stem with Greek letter</b>	<b>Different INN</b>



# Need for naming SBPs

It is the near universal opinion of regulatory bodies that switching arbitrarily between SBPs and their reference product or between SBP and SBP without medical supervision is undesirable.

Means to distinguish SBPs from each other ?

As prescription by nonproprietary name is common, and in some countries encouraged, the issue of the naming of SBPs does affect the INN Programme





# Naming SBPs an INN issue?

Naming SBPs directly affects the purposes of the WHO INN Programme in two ways:

- 1.If the reference and SBP INNs are the same, it may make substitution of SBPs for the reference substance more likely (not less) and, worse still, the substitution for one SBP by another.
- 2.If individual regulatory bodies develop their own naming policy for SBPs, there will a diversity in names, not “a unique name that is globally recognised”.



# Global name versus national names?

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epoetin alfa... epoetin lambda

tbo-filgrastim teva-aflibercept ado-trastuzumab emtansine

Japan            bs + identifier for biosmilars

Australia        sim + qualifier for biosmilars

and...



# Proposed INN naming of SBPs

It is therefore under discussion a proposal that all SBPs should be clearly identified:

1. All SBPs should have the INN of the reference product as the first part of the name. This effectively and unambiguously identifies the reference product for that SBP.
2. The second part should identify the medicine as a SBP and uniquely identify the product.



# Proposed INN naming of SBPs

There has also been some discussion about how the naming of SBPs should be implemented. The most viable options are:

1. The second part of the name is assigned by the INN Programme according to an agreed policy;
2. The INN Programme produces an advice document laying out an agreed naming scheme which may be applied by national regulatory authorities.



# Conclusion

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The naming of SBPs is an issue that does need to be addressed globally, and soon - while the number of registered SBP's is relatively small.

The WHO INN Programme has a clear mandate.

Global name to protect patient safety.

# Current challenges

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- The complexity of substances
- The number-induced difficulty
- The emerging of new types of substances (new policies?)
- Identifier for SBP? International set of standards?



# Thank you-спасибо

*Merci! Obrigado ! Gracias 谢谢! ありがとう ! ARIGATOU ! Danke! Dziękuję! Dank je / u!  
Mulțumesc! Teşekkür ederim! Tack!Tack så mycket Grazie! Kiitos! תודה  
!תקלTakk! d'akujem, d'akujem vám ; Hvala! شكرًا shokran Ευχαριστώ! 감사합니다  
Děkuji! Tak skal du have! Dankon! Hvala, Hvala lepa, Najlepša hvala Gràcies!  
Faleminderit Hvala! Ačiū, De'koju, Labai ačiū ขอบคุณ ใจ ; ขอบคุณ ใจ มาก (khàwp khun) ;  
(khàwp khun mâak) shukrīya (شكريبه) (بهت) bahut) Cảm ơn cô ; Cảm ơn cô nhiều;  
Благодаря!Благодаря! Obrigado!" Gracias Pakka pé! baie dankie ; Takk fyri! Sipas  
dekem !متشكروم! Благодарам! Hvala Vam! V Teşekkür Paldies!Pateicos! /  
Tencinu! Terima kasih Дуже дякую ;Дякую ; Спасибі! Баярлалаа ; Гялайлаа ;  
Танд иx баярлалаа Terima kasih धन्यवाद (dhonyobād) Salamat! Trugarez ! Mersi  
!Trugarez Danke!*

- <http://mednet.who.int/>
- [innprogramme@who.int](mailto:innprogramme@who.int)
- <http://www.who.int/medicines/services/inn/en/index.html>

