



## WHO International Standards and Reference Preparations for Cytokines and Growth factors

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The ability to quantify the activity of cytokines is an essential part of experimental and clinical investigation and is largely dependent upon the availability of suitable cytokine standards and reference reagents. The International Cytokine and Interferon Society (ICIS) Standards Committee was established to make recommendations regarding interferon and cytokine standards and standardization to the ICIS membership, and thereby to the international cytokine scientific community. The Committee works closely with the World Health Organization (WHO), the National Institute for Biological Standards and Control (NIBSC), the U.S. National Institutes of Health (NIH), the Biodefense and Emerging Infections Resources Repository (BEI Resources), pharmaceutical manufacturers, and regulatory agencies. The Committee includes members from several of these organizations. The role that the Committee plays as a source of information and recommendations to the ICIS membership, and to the international cytokine scientific community as a whole, is very much dependent upon suitable standards and reference materials being made available by the NIBSC. Similarly, the Standardization and Nomenclature Committee of the ICIS reviews the need for cytokine standards and their usage. With the expanding role of cytokines and growth factors in the development and manufacture of biotechnology derived products e.g., monoclonal antibodies targeting cytokines/growth factors, biosimilar medicines, cell and/or gene therapy products, the need for suitable standards is increasing.

The accompanying Table lists WHO International Standards (IS), WHO reference reagents (WRR) and other cytokine and growth factor standards available from the NIBSC. ISs and WRRs are publicly available reference standards with defined units (International Unit) established by the WHO Expert Committee on Biological Standardization. Lyophilised and formulated to ensure long term stability, they serve as 'primary' standards for bioactivity and for calibration of secondary reference standards. The use of IS and WRR to calibrate commercially available or laboratory made reagents including immunoassays where feasible, as per WHO recommendations, facilitates comparisons of data between assays, different laboratories, and individual studies allowing global harmonisation.

## Cytokine and growth factor standards and reference reagents available from the National Institute for Biological Standards and Control

A wide range of WHO International Biological Standards and reference materials are available for the calibration of assays of therapeutic substances and immunoassays and bioassays used in basic research. These materials are available from Standards Processing Division, National Institute for Biological Standards and Control (NIBSC), Blanche Lane, South Mimms, Potters Bar, Herts EN6 3QG, UK. The NIBSC does not charge for these materials, however there is a handling charge to cover the costs of administration, storage, and dispatch. The handling charge is currently £120 per ampoule. A comprehensive catalogue of reference materials is available from the above address or can be accessed online via the NIBSC website ([www.nibsc.org/products](http://www.nibsc.org/products)).

### Human Cytokine Standards and Reference Reagents

Preparation <sup>1</sup>	Product Code	Status <sup>2</sup>
Interleukin 1 alpha	86/632	1 <sup>st</sup> IS
Interleukin 1 beta	86/680	1 <sup>st</sup> IS
Interleukin 2	86/500	2 <sup>nd</sup> IS
Interleukin 3	91/510	1 <sup>st</sup> IS
Interleukin 4	88/656	1 <sup>st</sup> IS
Interleukin 5	90/586	WRR
Interleukin 6	89/548	1 <sup>st</sup> IS
Interleukin 7	90/530	WRR
Interleukin 8	89/520	1 <sup>st</sup> IS
Interleukin 9	91/678	WRR
Interleukin 10	93/722	WRR
Interleukin 11	92/788	WRR
Interleukin 12	95/544	WRR
Interleukin 13	94/622	WRR
Interleukin 15	95/554	WRR
Interleukin 17	01/420	WRR
Interleukin 18	03/200	WRR
M-CSF	89/512	1 <sup>st</sup> IS
G-CSF	09/136	2 <sup>nd</sup> IS
G-CSF(pegylated)	12/188	1 <sup>st</sup> IS
GM-CSF	88/646	1 <sup>st</sup> IS
Leukemia inhibitory factor	93/562	WRR
Oncostatin M	93/564	WRR
Stem cell factor	91/682	WRR
Flt 3 ligand	96/532	WRR
Bone morphogenetic protein-2	93/574	WRR
RANTES	92/520	RR
MCP-1	92/794	RR
GRO-alpha	92/722	RR
IFN alpha leukocyte	94/784	1 <sup>st</sup> IS
IFN alpha 1 (D)	83/514	1 <sup>st</sup> IS
IFN alpha 1/8	95/572	1 <sup>st</sup> IS
IFN alpha 2a	95/650	2 <sup>nd</sup> IS
IFN alpha 2b	95/566	2 <sup>nd</sup> IS
IFN alpha 2c	95/580	1 <sup>st</sup> IS
IFN alpha n1 lymphoblastoid	95/568	2 <sup>nd</sup> IS
IFN alpha n3 leukocyte	95/574	1 <sup>st</sup> IS
IFN alpha consensus	94/786	1 <sup>st</sup> IS
IFN omega	94/754	1 <sup>st</sup> IS
IFN beta	00/572	3 <sup>rd</sup> IS
IFN beta ser17	00/574	RR
IFN beta fibroblast	00/576	RR
IFN gamma	87/586	RR
IFN gamma leukocyte	82/587	BWS
IFN lambda1	10/176	WRR
TGF beta 1	89/514	RR
TGF beta 2	90/696	RR
TGF beta 3	09/234	1 <sup>st</sup> IS
Thrombopoietin	03/124	RR
TNF alpha	12/154	3 <sup>rd</sup> IS
TNF beta	87/640	WRR
TRAIL	04/166	WRR

## Human Growth Factor Standards and Reference Reagents

Preparation <sup>1</sup>	Product Code	Status <sup>2</sup>
Basic Fibroblast Growth Factor	90/712	1 <sup>st</sup> IS
Brain-derived neurotrophic factor	96/534	WRR
Ciliary Neurotrophic Factor	94/684	WRR
Epidermal Growth Factor	91/530	1 <sup>st</sup> IS
Epidermal Growth Factor (1-52)	91/550	WRR
Hepatocyte Growth Factor	96/564	WRR
Hepatocyte Growth Factor precursor	96/556	1 <sup>st</sup> IS
Keratinocyte Growth Factor	03/150	WRR
Keratinocyte Growth Factor (24-163)	03/148	WRR
Leptin	97/594	1 <sup>st</sup> IS
Nerve Growth Factor	93/556	WRR
Neurotrophin-3	98/718	RR
Platelet derived Growth factor BB	94/728	1 <sup>st</sup> IS
Vascular Endothelial Growth Factor 165	02/286	WRR

## Murine Cytokine Standards and Reference Reagents

Preparation <sup>1</sup>	Product Code	Status <sup>2</sup>
GM-CSF	91/658	RR
Interleukin 1- $\alpha$	93/672	RR
Interleukin 1- $\beta$	93/668	RR
Interleukin 2	93/566	RR
Interleukin 3	91/662	RR
Interleukin 4	91/656	RR
Interleukin 6	93/730	RR
Interleukin 7	93/740	RR
Interleukin 9	93/504	RR
Leptin	97/626	IS
TNF- $\alpha$	88/532	RR

## Standards for Cytokine Antagonists

Preparation <sup>1</sup>	Product Code	Status <sup>2</sup>
Etanercept	13/204	1 <sup>st</sup> IS
Infliximab	16/170	1 <sup>st</sup> IS

<sup>1</sup>All preparations listed above are rDNA derived unless specified;

<sup>2</sup> IS - International Standard; WRR - WHO Reference Reagent; RR – NIBSC Reference Reagent; BWS – British Working standard; WS – Working standard

## About the National Institute for Biological Standards and Control

The [National Institute for Biological Standards and Control \(NIBSC\)](#) is a global leader in the standardisation and control of biological medicines, playing a major role in assuring the quality of biological medicines worldwide.

NIBSC is a centre of the Medicines and Healthcare products Regulatory Agency which also includes CPRD and MHRA. The Medicines and Healthcare products Regulatory Agency is an executive agency of the Department of Health.