

Indian Pharmacopoeia Commission: Structure and Role in Formulation of IP and NFI

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Abstract—This article briefly reviews the role of Indian Pharmacopoeia Commission (IPC) for publications of Indian Pharmacopoeia (IP) and National formulary of India (NFI) to some of these anticipated changes, informs constituents about how they can remain updated about progress and upcoming modifications to official texts, and invites participation in the standards-setting process, which are helpful to the practitioners, researchers, educators and policy makers in the field of health care profession.

Keywords—Addendum, Indian Pharmacopoeia, Monograph, National Formulary of India.

I. INTRODUCTION

THE Government of India (GOI) was established a separate, dedicated, autonomous institution in the form of the Indian Pharmacopoeia Commission (IPC) in 2005 to deal with matter relating to timely publication of the Indian Pharmacopoeia (IP) is official book of standards for drug included there in, under the Second Schedule of the Drugs and Cosmetics Act, 1940 so as to specify the standards of identify, purity and strength of the drugs imported, manufactured for sale, stocked or exhibited for sale or distributed in India [1]. The mandate of the Commission is to perform, inter-alia, functions such as revision and publication of the IP and National formulary of India (NFI) on a regular basis besides providing IP reference substances and training to the stakeholders on Pharmacopoeial issues. The IPC has become fully operational from 1st January, 2009 as an Autonomous Body, fully financed by GOI with specific budgetary allocations under administrative control of the Ministry of Health and Family Welfare (M/o H&FW). The IPC is a three-tier structure consisting of 25 General Body, 13 Governing body, and 15-23 Scientific Body members. Secretary-cum-Scientific Director is the member secretary of all three bodies of IPC. The Secretary, M/o H&FW is the Chairperson and the Chairman-Scientific Body is the Co-Chairman of the Commission. Presently Dr G. N. Singh is the Secretary-cum-Scientific Director of the Indian Pharmacopoeia Commission has been discharging the functions and duties of Chief Scientific and Executive Officer since January, 2009 [2].

The goal of IPC is to promote public health by establishing and disseminating officially recognized standards quality for and authoritative information about the use of medicines and health care technologies by health care professionals, patients,

and consumers. Based on current facilities and congenial working scientific environment, the IPC is ready to perform scientific analytical validation of Drugs and Pharmaceuticals as an Independent Body whose results are unbiased, without conflict of interest and accepted by National/International bodies. Moreover, the main objectives of IPC are to develop comprehensive monographs for drugs to be included in IP, to accord priority to monographs of drugs included in the National Essential Medicines List and their dosage forms, to collaborate with other countries pharmacopoeias and International Pharmacopoeia and to organize educational programs and research activities for spreading and establishing awareness on the need and scope of quality standards for drugs and related articles/materials [3].

The IPC also provides IP Reference Substances which act as a finger print for identification of an article under test and its purity as prescribed in IP. IP standards are authoritative in nature. They are enforced by the Regulatory authorities for quality control of medicines in India. During Quality Assurance and at the time of dispute in the court of law the IP standards are legally acceptable. The work of the IPC is performed in collaboration with members of the Scientific Body, subject experts as well as with representatives from Central Drugs Standard Control Organization (CDSCO), State Regulatory authorities, specialist from Industries, Associations, Councils, and from other Scientific and Academic Institutions. IP contains a collection of authoritative procedures of analysis and specifications for Drugs. The IP, or any part of it, has got legal status under the Second Schedule of the Drugs & Cosmetics Act, 1940 and Rules 1945 there under. As per the policy of IPC, IP monographs are not framed to detect all possible impurities. The prescribed tests are designed to determine impurities on which attention are required to be focused, to fix the limits of those that are tolerable to a certain extent, and to indicate methods for ensuring the absence of those, that are undesirable. It is, therefore, not to be presumed that the impurities can be tolerated because they have not been precluded by the prescribed tests. Till date total seven IP editions and their supplements/addendums published by IPC; and also initiated to publish fourth edition of NFI-2011 and to be fifth edition NFI-2015 [4].

Distinction exists between Pharmacopoeial Standards and Manufacturer's release specifications. Pharmacopoeial standards are publicly-available compliance document that provide the means for an independent check about the quality of a product, all time during its shelf-life. To ensure compliance related to pharmacopoeial requirements, the

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manufacturer's specifications may need to be more exacting than corresponding pharmacopoeial specifications.

II. HISTORY OF IP

The history of IP began in the year 1833 when a committee of the East Indian Company's Dispensary recommended the Publication a Pharmacopoeia and Bengal Pharmacopoeia and General Conspectus of Medicinal Plants was published in 1844, which mainly listed most of the commonly used indigenous remedies. That was followed by IP-1868, which covered both the drugs of British Pharmacopoeia (BP) 1867 and indigenous drugs used in India, with a supplement published in 1869 incorporating the vernacular names of indigenous drugs and plants. However, from 1885 the BP was made official in India. A drug Enquiry Committee appointed in 1927 by the government recommended the publication of a National Pharmacopoeia. In year 1944 GOI asked Drug Technical Advisory Board to prepare the list of drug which was use in India having sufficient medicinal value to justify their inclusion in official pharmacopoeia. The list of drugs which are not included in the BP along with standards to secure their usefulness, tests for identity and purity was prepared by the committee and was published by the Government under the name the Indian Pharmacopoeia list 1946. The committee constituted under the chairmanship of Sir RN Chopra along with other nine members prepared the list of drugs such as substances included in BP, new 48 monographs for crude drugs, chemicals and their preparations also drugs of plant origin 90, drugs of animal origin 10, biological products 05, insecticides 07, colouring agents 03, synthesis 05, miscellaneous 15 and drug for veterinary use 02. Most of the crude-drugs included in that list are still in IP [5].

TABLE I
LIST OF PUBLICATIONS OF VARIOUS EDITIONS OF IP

IP Edition	Supplement/ Addendum	Chairman
First-1955	1960	Dr. B.N. Ghosh
Second-1966	1975	Dr. B. Mukerji
Third-1985 (Volume 2)	1989 & 1991	Dr Nitya Nand
Fourth-1996 (Volume 2)	2000, 2002, 2005 (Veterinary 2000)	Dr Nitya Nand
Fifth-2007 (Volume 3)	2008	Mr .Prasanna Hota (until 30 October 2006) and Mr. Naresh Dayal (from 31 October 2006)
Sixth-2010 (Volume 3)	2012	Mr. P. K. Pradhan
Seventh-2014 (Volume 4)	2015	Mr. Keshav Desiraju (until February 2014) and Mr Lov Verma (February 2014 onward)

After independence, the IP Committee was constituted by GOI on 23rd November 1948 for publication of IP as its main function. Central Indian Pharmacopoeia Laboratory (CIPL) was established in 1965 under Directorate General of Health Services (DGHS), M/o H&FW as sub-ordinate office/laboratory of CDSCO. Drugs Controller was Member

Secretary and Director CIPL was member of IP Committee. Several other sub-committee were appointed to assist the IP committee such as Clinical, Pharmacology, Biological, Pharmacognosy, Pharmacy and Pharmaceutical sub-committee were important amongst the committees helped in compilation of draft-monographs of IP. The IP editions and its Supplements or Addendum are listed in Table I. Thus, the first edition of IP was published in 1955 and that was written in English. The official titles of the monographs were mentioned in Latin and covered total 986 monographs. Furthermore, since many new drugs were introduced to the market that was felt necessary to provide standard for these drugs, in this context the supplement to first edition IP was published in 1960. Moreover, second edition of IP was published in 1966 contains 890 monographs and 41 appendices were several changes has been made such as the title of the monographs are written in English not in Latin and naming style of monographs also been changed. The title mentioned the name of drug first, category of drug indicated at the end and doses were given in metric system. Preparations of the drugs are followed immediately after the parent monograph of the drug. During preparation of second edition 274 monographs from IP-1955 and its supplement 1960 were deleted whereas 93 new monographs were added in the second edition IP-1966, such new addition monographs consist of herbal drugs, antibiotics etc. In continuation since many new drugs were introduced in the medical practice after the publication of second edition IP-1966, it was very essential to provide them the official standards and to amend second edition. Thus, published the supplement of IP in 1975 contains 126 new monographs and also 250 new monographs of second edition have been amended. Only one monograph on Cholera vaccine has been deleted from that supplement. Changes and addition in the second edition and its supplement contains monographs on capsules and eye ointment has been re framed and sterility test for eye ointment first time incorporated. New analytical techniques such as Thin Layer Chromatography, Gas Liquid Chromatography and IR spectroscopy have been added [6].

The IP committee for preparation of third edition was reconstituted under the chairmanship of Dr Nitya Nand Director of Central Drug Research Institute, Lucknow in June 1978 and published the third edition IP in 1985 in two volumes along with the nine appendices that contains 261 new monographs and 450 monographs included in second edition have been deleted from this third edition. The main important features of IP-1985 was IUPAC nomenclature used for the organic chemical drugs, analytical techniques like electrophoresis, flurometry, flame photometry, photometric haemoglobinometry has been given first time official recognition where as instrumental techniques such as UV spectroscopy, gas chromatography, fluorescence and atomic absorption spectrophotometry have been use for the analysis, dissolution test for tablet dosage form and limit test for microbial contamination of pharmaceutical aids and some liquid formulations mentioned, the appendices for pharmaceutical containers, water for pharmaceutical use

design and analysis of biological assay have been annexed in the third edition IP-1985. Addendum-I as a supplement of IP-1985 third edition, published in 1989 contained new 46 monographs and amended 126 monographs of third edition IP. Addendum-II as a supplement was published in 1991 and is effective from 1st January 1992 it covers 62 new drugs and amendment to 110 monographs of the third edition. An appendix on high performance liquid chromatography (HPLC) and determination of water by azeotropic distillation have been added to the third edition IP-1985 [7].

Fourth edition of IP was published in 1996 and has been made effective from 1st December 1996 it contains 1149 monographs and 123 appendices. The fourth edition includes 294 new monographs while 110 monographs have been deleted from third edition. A good number of general monographs like creams, eye drops, gels nasal preparations, oral liquids, pessaries, and suppositories have been incorporated. Important among the new appendices added to the fourth edition are Biological indicators, jelly-strength, osmolarity, particulate matter, contents of packaged dosage form etc. Test for bacterial endotoxins as a substitute test for the pyrogens and the extensive use of HPLC for analysis of drug-substances and few of the salient features of fourth edition of IP-1996. Addendum-I as a supplement of fourth edition, published in 2000 contained 42 new monographs have been added to IP-1996 through this addendum. The Carbamazepine monograph have undergone major changes while, bacterial endotoxin test for pyrogens has been replaced by extensively revised version to the earlier gel clot test. This has come into force from December 31, 2000. Addendum-II as a supplement of fourth edition IP-1996, published in 2002 and has come into effective from 30th June 2003, new 19 monographs have been added through this addendum to IP-1996. In view of the continuing rapid increase in the range of drugs produced in India, the IP 1996, its Addendum 2000, Supplement 2000 for Veterinary Products and Addendum 2002 were published. First time emphasis has given to veterinary products also in veterinary supplement 2000 to IP-1996. First time the monographs on Anti-Retroviral Drugs were introduced in the Addendum-2002. The IP Committee decided to delete the obsolete or less used product monographs and added monographs based on the therapeutic merit, medical need and extent of use of such articles in the country [8].

III. ROLE OF IPC FOR PUBLICATION OF IP

The IPC was established in year 2005, dissolving the existing Indian Pharmacopoeia Committee and started working in existing Central Indian Pharmacopoeia Laboratory (CIPL) with its Director as Member Secretary. The Addendum 2005 was published by IPC which included a large number of antiretroviral drugs and raw plants commonly used in making medicinal products not covered by any other pharmacopoeias, which attracted much global attention. It provided systematic approach and practices for publication of fifth edition IP-2007 with three volumes containing 271 new monographs with focus on those drugs and formulations that cover the National

Health Care Programmes and the National Essential Medicines. Addendum 2008 of IP-2007 containing 72 new monographs and amendments published in the year 2008. Ministry of Health and Family Welfare, Government of India submerged the existing CIPL along with IPC as a fully financed autonomous body from 1st January, 2009 located at NCR region in the Ghaziabad, Uttar Pradesh (Fig. 1).

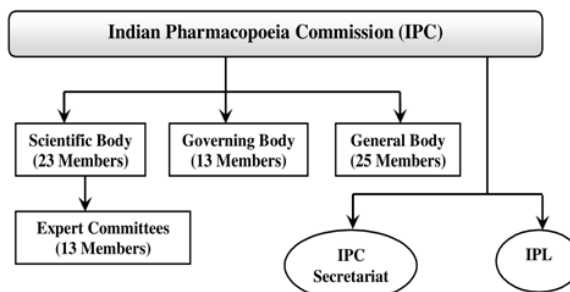


Fig. 1 Structure of Indian Pharmacopoeia Commission

The IPC is a three-tier structure comprising of the General Body of 25 members, Governing body of 13 members and Scientific Body of 15-23 members from different related scientific fields. Secretary-cum-Scientific Director of IPC is the Member Secretary of all three bodies of IPC. The Secretary, M/o H&FW, is the Chairman and the Chairman-Scientific Body is the Co-Chairman of the Commission. The Secretary-cum-Scientific Director is the Chief Scientific and Executive Officer of the Commission [9].

The IPC Secretariat and Indian Pharmacopoeia Laboratory (IPL) staffs, with the support of different advisory experts committee and expert members of the scientific body have examined the suitability of the standards for the sixth edition IP published in 2010. IP-2010 contained total 2000 monographs including 287 new monographs and more than 600 updated monographs. Sixth edition IP-2010 comprises of three volumes. Each volume has got different features. Volume I contains Notices; Preface; About IPC; Acknowledgements; Introduction; General Chapters and Reference Data. Volume II contains General Notices; Dosage Forms (General Monographs); Drug Substances, Dosage Forms and Pharmaceutical Aids (A to M). Volume III contains General Notices; Drug Substances, Dosage Forms and Pharmaceutical Aids (N to Z); Vaccines and Immunoserum for Human Use; Herbs and Herbal Products; Blood and Blood-related Products; Biotechnology Products; Veterinary Products and Index. The scope of the Pharmacopoeia has been extended to include products of been extended to include products of biotechnology, indigenous herbs and herbal products, Veterinary vaccines and additional antiretroviral drugs and formulations, inclusive of commonly used fixed dose combinations. Standards for new drugs and drugs used under National Health Programmes are added in the sixth edition IP-2010 and drugs as well as their formulations not in use now a day are omitted from that sixth edition. The numbers of monographs of Excipients, Anticancer drugs, Herbal products

and Anti HIV drugs have been increased in sixth edition. Monographs of Vaccines and Immunosera are also upgraded. A new chapter on Liposomal products and a monograph of Liposomal Amphotericin B injection is an added advantage in view of latest technology adopted for drug delivery. A chapter on Nuclear Magnetic Resonance (NMR) is also incorporated in Appendices. The chapter on microbial contamination is also updated to great extent to harmonize with prevailing international scenario. Addendum 2012 to the IP-2010 was published which had taken care of the Amendments to IP 2010 along with 52 new monographs [10].

The seventh editions, IP-2014 with four volumes was released on 4th November, 2013 and has become official from 1st April, 2014. The IP-2014 published in accordance with the principles and designed plan decided by the Scientific Body of the IPC. The standards prescribed in seventh edition are encouraged to adhere with the concept of harmonization, keeping in view the technological status for manufacture and analysis of drugs and pharmaceuticals in the country without compromising with the quality of the products. The IP-2014 incorporates 2548 monographs of drugs out of which 577 new monographs, 134 API monographs, 161 formulations monographs, 18 excipient monographs, 43 NDS monographs, 10 antibiotic monographs, 19 anticancer monographs, 11 antiviral monographs are included in this edition. Also 31 herbal monographs, 05 monographs on Vaccine and Immunosera for human use, 06 monographs on insulin products and 07 monographs on biotechnology products are included. Moreover, 19 new General Chapters and about 200 new IR spectra's are also added in seventh edition. The first time in IP introducing 19 new Radiopharmaceutical Monographs with one General Chapter on Radiopharmaceutical preparations. There is separate volume of veterinary products for easy access such as 143 monographs on veterinary products along with 16 appendices/General chapter on veterinary products are also included. Now total number of IP Standards is reaching almost 3000 which are almost at par with other international Pharmacopoeias and comprising different categories of drugs and appendices [11]. However, based on scientific inputs, some monographs, appendices needed corrections, which are mentioned in the Errata-001 and 002 for IP-2014 was issued in October, 2014 by IPC, such minor corrections to be appear in IP Addendum-2015 [12]. The IPC 29th Scientific Body meeting on 3rd December, 2014 launched IP Addendum-2015 to IP-2014 [13]. In continuations the IPC have make the Road Map for Addendum-2016 of seventh edition IP2014 and it to be release in the year 2016 [14].

Hence, the IP been published in accordance with the principles and designed plan decided by the Scientific Body of the IPC. To establish transparency in setting standards for new edition and addendum of IP, the contents of new monographs, revised appendices and others information have been publicized on the website of the IPC, besides following conventional approach of obtaining comments. The feedback and inputs were reviewed by the relevant Expert Committee to ensure the feasibility and practicability of the standards and

methods revised. The principle of "openness, justice and fairness" is kept in mind during compiling and editing the contents of new edition. Public review and comment process for standards development related to IP have given special attention to incorporate comments from stakeholders. The methodology adopted is shown in Fig. 2 [15].

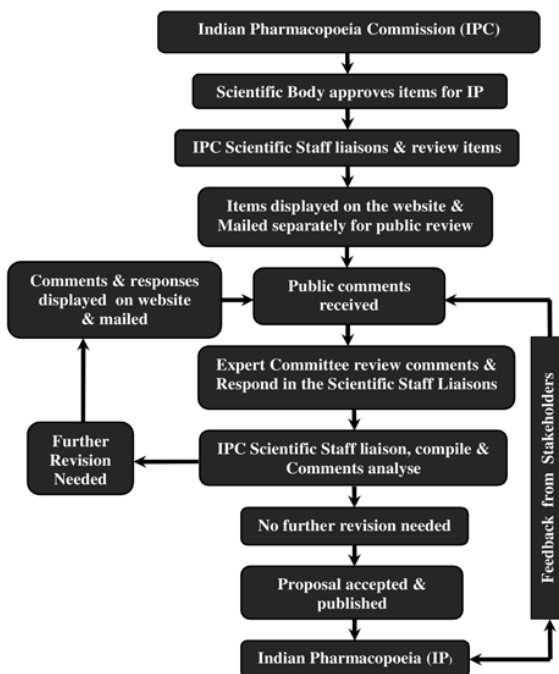


Fig. 2 IP Monographs Development Process

IV. NATIONAL FORMULARY OF INDIA

Multiplicity of drugs, their several preparations and continuous flow of new drugs in the medical practice has made it difficult even for a qualified and experienced physician to discriminate the choice of drugs. Drug interaction, resistance, cumulative effects are other factors, which the physician has to take into consideration while treating the patients. Thus, for the guidance of medical practitioners, medical students and pharmacists in hospitals and in sales departments, National Formulary of India (NFI) have been formulated.

The First edition of NFI was published by GOI, Ministry of Health. Since, many new drugs had come into use, after the first edition NFI publication. Hence it becomes essential to revise the formulary and bring it up to date. Thus, the Second edition of NFI was published 1966 contained 206 formulations of first edition have been deleted and 219 formulations of new drugs have been added to second edition. In the NFI-1966 separate pediatric section and chapter on diet has been added to formulary. Methods of treatment of poisons, list of diagnostic agents, list of proprietary and trade names are the other features of second edition. While compiling the valuable information, BP, USP, British national Formulary, National Formulary of United States, several renewed teacher in the

profession, consulting physicians have been consulted. Furthermore, revised third edition of NFI published in 1979, it contains 255 deleted formulations of NFI-1966, while added 342 new formulations. Separate chapters on drug-interactions, drug dependence, prescription writing are the special feature of third edition NFI-1979. However, as more than three decades have elapsed since the publication of the last edition of the NFI, it is to be expected that the fourth edition of NFI has been published in 2011 by the IPC it would have many distinct features to promote the rational use of medicines in the country. The IPC with its mission to be one of the leading scientific institutions under the central government puts stress on keeping transparency, accountability and punctuality and the publication of the NFI. The formulations included in the formulary and the ingredients thereof should conform to the standards laid down in the current edition of the IP. If no standards are specified in the current edition but are specified in the immediately preceding edition of the IP then these standards would apply. In respect of drugs for which no standards have been laid down in the IP, these would have to conform to the standards laid down in the official pharmacopoeia of any other country wherein they are included. The provisions of the Drugs and Cosmetics Act and the Rules made there under including those relating to labeling and conditions of storage should be observed [16].

Moreover, the IPC asked to health care professional and other stakeholders to send their feedback on the draft content of NFI fifth edition which is scheduled to be published in 2015. The Contents of NFI-2015 may be as following order: Disclaimer, List of Contents, Preface, Introduction, List of Medicines in NFI and Omitted Medicines, Common Abbreviations, General Advice to Prescribers, Chapter 1 to 10, Chapter 11 to 21, Chapter 22 to 33, All Appendices 1-22 except Appendix 8, Appendix 8 Domiciliary Care of Seizures, Part 1 of Appendix 17 ADR Reporting Form for Health Professionals, Part 2 of Appendix 17 ADR Reporting Form for Consumers, Index and last Feed-back Form [17].

V. CONCLUSION

This article summarizes the structure, work plan of the IPC for the formulation and publish the IP. The IP is an official document meant for Quality Control and Assurance of Pharmaceutical products marketed in India by way of contributing on their safety, efficacy and affordability. Monographs of the IP updated on the basis of several factors, including Expert Committee and staff resources and focus, and the number and type of public comments received in response to a particular revision proposal. IPC also involved in the formulation of NFI-2011 and to be NFI-2015, that are useful to the healthcare professional and pharmacist for guidance of new medicine in practice. Hence, IPC having important role in the publication of IP and NFI that may be helpful to the practitioners, researchers, educators and policy makers in the field of medicine.

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