REPUBLIC OF THE PHILIPPINES

Intellectual Property Office of the Philippines

REVISED GUIDELINES ON THE EXAMINATION OF PHARMACEUTICAL APPLICATIONS INVOLVING KNOWN SUBSTANCES

(QUAMA Guide)

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A. INTRODUCTION

1. SCOPE

The QUAMA Guide is complementary to the practices and procedures as set out in the Bureau of Patents Manual of Substantive Examination Practice (MSEP). It provides the methodology to be observed by BOP patent examiners in the examination of patent applications for drugs and medicines, pursuant to the amendments to the Intellectual Property Code brought by Republic Act 9502 (Universally Accessible Cheaper and Quality Medicines Act of 2008) and its Implementing Rules and Regulations (Joint DOH-DTI-IPO-BFAD Administrative Order No. 2008-01).

Because of public health considerations, applications involving drugs or medicines involving known substances are granted letters patent only when they satisfy the eligibility standard requiring that the subject matter must not fall in any of the enumeration of non-patentable inventions while meeting the criteria of novelty, inventive step and industrial applicability. Thus, an invention must pass all criteria, and knowledge that is or has become part of public domain, whether explicit or inherent, should not be allowed to crawl back into the patent space.

Recognizing that identical provisions are contained in the sections on non-patentable subject matter and inventive step, the QUAMA Guide provides an explanation on the coherent manner of assessing the patent application against the patent eligibility standard and the patentability criterion of inventive step, consistent with generally accepted principles and practices in patent examination. As demonstrated in the examples, the QUAMA Guide adopts the doctrine of inherency in its expanded sense in order to articulate on the meaning of "mere discovery." Subjecting the term "mere discovery" to inherency analysis clarifies any ambiguity and provides a more definitive methodology for examiners.

The guidelines set out below, contains, where feasible, some illustrations. However, the same is merely explanatory, and to be used as reference, consistent with the general policy rationale in RA 8293 that an effective intellectual and industrial property system is vital to the development of domestic and creative activity on one hand, and with the principle in RA 9502 that places emphasis on the non-eligibility of mere discoveries on the other. It is important to note that each application must be examined on a case-by-case basis and with in-depth analysis of the above considerations. The present QUAMA Guide is dynamic and this Office shall update the same as needed.

2. DEFINITION OF TERMS

a. ***"Drugs and medicines"*** refer to any chemical compound or biological substance, other than food, intended for use in the alleviation of symptoms and the treatment, prevention or diagnoses of diseases in humans or animals, including but not limited to:

(1) Articles recognized in the current official United States Pharmacopoeia-National Formulary (USP-NF), official Homeopathic Pharmacopoeia of the United States, Philippine Pharmacopoeia, official Philippine National Drug Formulary(PNDF), British Pharmacopoeia, European Pharmacopoeia, Japanese Pharmacopoeia, Indian Pharmacopoeia, any national compendium or any supplement to any of them;

(2) Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or animals;

(3) Articles other than food intended to affect the structure or any function of the human body or animals;
(4) Articles intended for use as a component of articles specified in clauses (1), (2), or (3) not including devices or their components, parts, or accessories; and
(5) Herbal and/or traditional drugs which are articles of plant or animal origin used in folk medicine that are:
  (i) Recognized in the Philippine National Drug Formulary Vol. I (Essential Drugs List);
  (ii) Intended for use in the treatment, cure or mitigation of disease symptoms, injury or body defects in humans;
  (iii) Other than food, intended to affect the structure or any function of the human body;
  (iv) In finished or ready-to-use dosage form; and
  (v) Intended for use as a component of any of the articles specified in clauses (i), (ii), (iii), and (iv).
(6) In case of conflicts, the BFAD drug classification will prevail.

b. Effective filing date refers to the priority date or filing date of the patent application

c. Known substance refers to a known chemical compound or biological substance, other than food

d. Nanotechnology is the study, design, creation, synthesis, manipulation, and application of functional materials, devices, and systems through control of matter at the nanometer scale (10^{-10}m) and the exploitation of novel phenomena and properties of matter at that scale.

e. New form refers to isomers, stereoisomers, polymorphs, metabolites, prodrugs, homologues, hydrates, acid addition salts, pure forms, new particle size of known pharmaceutical compounds; various derivatives of known chemical compounds such as esters, ethers, complexes and other derivatives thereof; compositions or formulations comprising the known compound. These compositions or formulations may comprise excipients or pharmaceutically acceptable carriers such as binders, diluents or fillers, stabilizing agents, disintegrants, and lubricants; or to combinations of known substances, including kits.

f. New use refers to first or further medical use of a known compound or composition.

g. Process refers to the preparation/method of manufacture/method of producing a product or composition.

h. QUAMA refers to RA 9502(Universally Accessible Cheaper and Quality Medicines Act of 2008).

3. PROVISIONS COVERED

Taking the cue from the DOHA Declaration, RA 9502, enacted on 06 June 2008, has amended the IP Code (RA 8293) in respect of pharmaceutical inventions. The law took effect on 4 July 2008.

The pertinent QUAMA provisions are found in Section 22.1 and Section 26, of the IP Code, as amended.

Section 22 of the IP Code, as amended, enumerates the following subject matters to be excluded from patent protection:

22.1 Discoveries, scientific theories and mathematical methods; and in the case of drugs and medicines, the mere discovery of a new form or new property of a known substance which does not result in the enhancement of the

known efficacy of that substance, or the mere discovery of any new property or new use for a known substance, or the mere use of a known process unless such known process results in a new product that employs at least one new reactant. "For the purpose of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations, and other derivatives of a known substance, shall be considered to be the same substance unless they differ significantly in properties with regard to efficacy;

22.2 xxx;
22.3 xxx;
22.4 xxx;
22.5 xxx;
22.6 xxx;

Section 26 of the IP Code, as amended, states that:

26.1 An invention involves an inventive step if, having regard to prior art, it is not obvious to a person skilled in the art at the time of the filing date or priority date of the application claiming the invention.

26.2 In the case of drugs and medicines, the mere discovery of a new form or new property of a known substance which does not result in the enhancement of the known efficacy of that substance, or the mere discovery of any new property or new use for a known substance, or the mere use of a known process unless such known process results in a new product that employs at least one new reactant. "For the purpose of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations, and other derivatives of a known substance, shall be considered to be the same substance unless they differ significantly in properties with regard to efficacy.

In relation to the above provisions, Section 22.3 of the IP Code is also relevant since it provides the legal basis of granting medical use claims in PH jurisdiction.

Section 22.3 of the IP Code, states that:

22.3 Methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body. ***This provision shall not apply to products and composition for use in any of these methods;***

4. GENERAL GUIDELINES

The following pharmaceutical patent applications involving known substances shall be examined under RA 8293 as amended by RA 9502, guided by the IRR and this QUAMA Guide.

a) PCT Route: PCT applications which have an effective filing date of 5 July 2008 onwards
b) Direct Route: Patent applications which have an effective filing date of 5 July 2008 onwards

The changes introduced by RA 9502 led to a substantive change in the patent eligibility of inventions in the pharmaceutical field. To have a meaningful interpretation of the QUAMA provisions during substantive examination, three (3) cases are contemplated, namely:

Case A : mere discovery of a new form or new property of a known substance which does not result in the enhancement of the known efficacy of that

substance;

Case B : mere discovery of any property or new use for a known substance; and

Case C : mere use of a known process unless such known process results in a new product that employs at least one new reactant.

The three cases enumerated above become material during non-patentable subject matter inquiry and assessment of inventive step requirement of drugs and medicines.

In case A, only the new form shall be considered because any claim to a property per se of an already known compound does not make such compound novel and/or inventive.

In case B, only the new use shall be subjected to requirements of patentability since the new use maybe based on the recognition of a previously unknown property of a known compound.

The flowchart for each Case provides clarity on the aspects that need to be addressed. It prescribes how to qualify a claimed new form, enhanced efficacy, new use as mere discoveries. It articulates and demonstrates the methodology to be observed by the examiners when examining pharmaceutical applications under the QUAMA provisions.

It is important to note that while the Doctrine of Inherency is adopted to articulate on the meaning of “mere discovery”, a new concept of its application to patentability requirements is introduced in this QUAMA Guide. Specifically, inherent disclosures shall be considered when assessing patent eligibility and inventive step, a different practice compared to other jurisdictions where such disclosures are considered during novelty assessment. Following this new concept, inherent new form or new use of a known substance would be considered as mere discoveries, hence not a patentable subject matter within the purview of the QUAMA provision. Moreover, a mere use of known process not resulting to a new product and not employing at least one new reactant is also considered as inherent, hence not a patentable subject matter in view of the QUAMA provision.

As regards "enhanced efficacy" criterion, this requirement shall be subjected using inherency principles as well. We note that in pharmaceutical field, it is typical that new forms will offer "enhanced efficacy", as a new property may be attributed to its new form. Where the enhanced efficacy inevitably and necessarily flows from the explicit disclosures of the prior art, the new form, even it exhibited an enhancement of known efficacy, should be ineligible for patent protection for being drawn to a mere discovery. For example, it is known that the enhanced efficacy of a racemic mixture of a compound with known chiral carbon is due to the properties of the active isomer and naturally, new salts of known compounds will be more stable than its parent compound.

Claims which are drawn to non-inherent new form of known compounds which resulted to non-inherent enhanced efficacy shall qualify as eligible subject matter. However, the existence of the enhanced efficacy should not be considered per se as demonstrating inventive step where a new form is rendered obvious to a person skilled in the art. This is because it is a well-accepted principle that without the exercise of any inventive ingenuity, any additional advantage, even if unexpected, could only be considered as a gratis effect which would inevitably have resulted from

the non-inventive activity. As such, there could be no invention in doing what was suggested in the prior art, even though the known efficacy is enhanced.

With regard to new medical use of a known compound, this use maybe based on the recognition of a previously unknown property of a compound, such property providing a valuable new technical effect and involving inventive contribution to the art. Where the new technical effect is found to be inherent in the prior art, a rejection under Section 22.1 should be made. On the other hand, a new use of a known substance which is not inherent in the prior art would be a patentable subject matter. It is worth keeping in mind that while it may pass the query on patent eligibility, it shall still be subject to the inventive step criterion.

The examples herein should be considered as illustrations of the guidelines set out in this QUAMA Guide when examining pharmaceutical patent applications involving known compounds under the QUAMA provision. Objective decision may be taken by the examiner taking into account the merits of each application.

5. BACKGROUND ON PHARMACEUTICAL INVENTIONS

For better understanding on the issues related to the patentability of pharmaceutical applications involving known substances, reference is made hereunder on claims which are usually filed for patent applications in pharmaceutical field.[1]

Generally, applications pertaining to pharmaceutical field relate to the following subject matter, but not limited to:

A. Physical Entity
   - new chemical compounds
   - formulations/compositions
   - combinations/dosage/dose
   - various forms of chemical compounds such as isomers, stereoisomers, homologues, polymorphs, metabolites, prodrugs, hydrates, acid addition salts, pure forms, new particle size
   - various derivatives of chemical compounds such as esters, ethers, complexes and other derivatives thereof
   - kits
   - product-by-process
   - selection inventions

B. Activity
   - process/method of manufacturing
   - new medical uses of known compounds

Similar to other fields of technology, pharmaceutical patent claims must meet the same requirements of novelty, inventive step and industrial applicability. In addition, the claims must be clearly defined and be supported by the description. Likewise, the invention must not fall under the excluded categories defined in Section 22.

Aside from the limitations brought by RA 9502, patenting in the medical field is also constrained by the exclusion from patentability of methods of treatment by surgery

[1]It is important to note that patent applications in the medical field which relate to the use of biotechnological inventions for medical purposes, i.e. gene therapy, are covered by a separate Examination Guidelines for Patent Applications relating to Biotechnological Inventions.

or therapy, or methods of diagnosis practiced on the human body under Section 22.3 of the IP Code.

The policy behind the exclusion of such methods is to ensure that those who carry out such methods as part of the medical treatment of humans or the veterinary treatment of animals should not be inhibited by patents.

5.1 Exclusions of Methods of Treatment

Methods of treatment not falling within the scope of the terms "therapy" and "surgery" are not excluded from patentability. Furthermore, claims to methods of diagnosis are objectionable only if they are performed directly on the human body or animal body.

To provide further clarification on the boundaries between the exclusion of methods of treatments from patents and the patentability of products and compositions used in such treatment, reference is made hereunder on specific details about this subject matter.

5.1.1 Method of Treatment by Therapy

"Therapy" is defined as "any treatment which is designed to cure, alleviate, remove or lessen the symptoms of, or prevent or reduce the possibility of contracting any disorder or malfunction of the animal body". Veterinary treatment of a sick or injured animal is also regarded as therapy.

The following drafts of claims are construed to define methods of treatment by therapy, and are thus excluded from patent protection in view of Section 22.3 of the IP Code:

i) Method of treating disease Y by administering (a therapeutically effective amount of) a substance or composition X
ii) The treatment of disease Y with substance X
iii) The use of substance X to treat medical condition Y
iv) Use of a substance or composition X for the treatment of disease Y
v) Substance X when used to treat medical condition Y
vi) The use of substance X as a pharmaceutical/antibacterial
vii) Use of a substance or composition X as a medicament for the treatment of disease Y

The above claims are considered as method of treatment, thus not allowed by express provision of law.

A claim to the use of a substance "as a pharmaceutical" or "as a medicament" is interpreted as a method claim to the use of the substance in therapeutic treatment, rather than simply a claim to its use in a pharmaceutical formulation.

Determining "Treatment by Therapy"

Section 22.3 has an intention of ensuring that those who carry out such methods as part of the medical treatment of humans or the veterinary treatment of animals should not be inhibited by patents, thus, a claimed method which does not have an impact on a medical practitioner's discretion is likely to fall outside the scope of Section 22.3.

The following specific examples will clarify what methods of treatment falls within the definition of "therapy".

Therapeutic and Non-Therapeutic Methods: Specific Examples

Therapeutic

i.) *Removal of parasites*. A method of treating or preventing infestation of internal parasites is considered as therapeutic as well as treatment of parasites residing on the skin of a human or animal. For example, treatment of head lice is a treatment by therapy.

ii.) *Oral Care.* Methods for the removal of dental plaque, or preventing the formation of plague have the effect of treating or preventing dental caries, thus therapeutic.

iii.) *Pain, smoking and addiction.* Irrespective of the origin of pain, discomfort or incapacity, its relief, by the administration of an appropriate agent, is to be construed as "therapy". Methods to stop smoking, among others as treatment of addiction or withdrawal symptoms are considered as therapeutic methods.

iv.) *Obesity.* A method in treating obesity is considered as therapeutic.

v.) *Contraception, abortion and fertility treatment.* A method of contraception, which is to be applied in the private and personal sphere of a human being, is not a patentable subject matter. Also, methods of abortion, termination of pregnancy or induction of labor are regarded as non-patentable treatments regardless of the reasons for performing these methods.

vi.) *New method, time, frequency or dosage of administration.* A medical use claim defined solely by *new method, time, frequency or dosage of administration* are construed to be methods of treatment directed at the activity of the doctor, thus not patentable under Section 22.3 of the IP Code. See also discussion in 5.2.2.

Non-therapeutic

i.) *Fatigue.* Reducing fatigue was not comparable with the relief of pain, thus, could be considered as non-therapeutic.

ii.) *Weight reduction.* A claim to a "method of improving the bodily appearance of a non-opiate-addicted mammal" relating to cosmetic weight loss only, is considered as non-therapeutic.

iii.) *Treatment of stock animals*. Methods of treating an animal in order to improve their meat or milk yields, to promote growth, to improve the quality of mutton or to increase the yield of wool; or other methods of measuring or recording characteristics of the animal body are patentable subject matter. For example, using a medication to increase milk production in cows maybe acceptable if it is shown that the success of the treatment is not a mere consequence of animal's state of health.

Some methods could be deemed as non-therapeutic or therapeutic depending on the nature of the steps involved in the method. As discussed below, if the method involves both non-therapeutic and therapeutic methods, and these are inevitably linked, a rejection under Section 22.3 is more likely to arise. Examples of these methods are:

Methods	Therapeutic	Non-therapeutic
i. Cosmetic method	Methods where the cosmetic and therapeutic aspects of the claimed method of protecting skin are "inevitably linked, such that each one necessarily develops together with the other and such that is impossible to separate them". For example:	Methods where treatments of the skin and hair are purely cosmetic. For example: • strengthening hair and using a composition to protect the lips from sunburn • methods of protecting the skin by simply blocking UV

	• methods of protecting the skin by blocking UV radiation with physiological effects. • use of composition for the local treatment of blackheads in the treatment of acne • treatment of dandruff, where the clinical presentation shows a link with seborrhoeic dermatitis, or it resulted from fungal and microbial infection	radiation • treatment of dandruff, where it resulted from simple scaling due to excessive exposure to sunlight, irritation of scalp due to over shampooing, frequent combing, use of certain cosmetic products, dusts and dirt
ii. Methods utilizing implanted devices	A method of operating a pacemaker in which its output to the heart is adjusted	A method concerning with the operation of a device without functional link between the claimed method and the effects produced by the device on the body, for example - a method of controlling the input energy to a pacemaker which does not affect the output to the heart.
iii. Treatments performed outside the body	Treatment of human or animal body tissues or fluids after they have been removed from said body and are returned to the same or any human/animal body. It may include: • treatment of blood or tissue by dialysis with the blood being returned to the same or any human/animal body	• A treatment practiced on a dead human or animal body. • Treatment of human or animal body tissues or fluids after they have been removed from said body as long as these tissues or fluids are not returned to the same or any human or animal body. An example is the treatment of blood for storage in a blood bank.

5.1.2 Method of Treatment by Surgery

Surgery is defined as the treatment of the body by operation or manipulation. It is not limited to cutting the body but includes manipulation such as the setting of broken bones or relocating dislocated joints, also referred as "closed surgery", and also dental surgery.

"Treatment by surgery" include those interventions which, whatever their specific purpose, give priority to maintaining the life and health of the human or animal body on which they are performed. As such, the definition of surgery includes "endoscopy, puncture, injection, excision and catheterization. However, methods involving relatively low levels of technical expertise (such as simple injection methods for taking blood samples or introducing compositions) would not be regarded as method of surgery. On the other hand, lumbar punctures to deliver epidural injections would fall as method of surgery.

Surgery defines the nature of the treatment rather than its purpose. Thus, e.g. a method of treatment by surgery for cosmetic purposes is excluded, as well as surgical treatment for therapeutic purposes or other non-therapeutic purposes such as sterilization.

A claimed imaging method, in which, when carried out, maintaining the life and health of the subject is important and which comprises or encompasses an invasive step representing a substantial physical intervention on the body and which entails a substantial health risk, even when carried out with the required professional care and expertise, is excluded from patentability as a method for treatment of the human or animal body by surgery pursuant to Section 22.3 of the IP Code.

5.1.3 Diagnostic Methods

Diagnostic methods likewise do not cover all methods related to diagnosis. Methods for obtaining information only (data, physical quantities) from the living human or animal body are not necessarily excluded by Sec.22.3 if the information obtained merely provides intermediate results, which on their own, do not enable a decision to be made on the treatment. Examples of such methods include X-ray investigations, NMR studies, and blood pressure measurements.

In order to be excluded from patent protection, a method should fall within the definition of a "method of diagnosis" and whether it is "practiced on the human or animal body". It is not dependent on who carries out the method. Such method can be practiced by medical practitioner, medicinal or non medicinal support staff, the patient himself or herself or an automated system.

Defining diagnosis and "practiced on the human or animal body"

Diagnosis is defined as the determination of the nature of a medical condition, usually by investigating its history, aetiology and symptoms and by applying tests. It includes a negative finding that a particular condition can be ruled out, as well as a positive identification of a disease.

Methods of diagnosis involves a number of steps characterized as follows:

(1) the examination and collection of data;
(2) comparison of the data with normal values;
(3) recording any deviation from the norm; and finally
(4) attributing the deviation to a particular clinical picture.

If a claimed method includes all these steps leading towards identification of a medical condition, it clearly falls within the definition of method of diagnosis. During examination, the examiner should be able to determine if the intermediate steps are implied.

Moreover, a diagnostic method, to be excluded, would generally have to be carried out on the living human or animal body. A method is excluded if all the technical steps as recited above are practiced on the human or animal body. Therefore, methods of *in vitro* diagnostic tests, performed on blood or other samples removed from the body, are patentable subject matter. A method carried out on a dead body, for example to determine the cause of death, is also patentable.

In most cases, the examination and collection of data (the first step) is the only one that may be "practiced on the body" and considered as the only technical step.

"To decide whether a particular step in a method is "practised on the human or or animal body", the key test is whether the step requires the presence of the patient to perform it. It is irrelevant whether the procedure is invasive, or capable of causing harm to the patient.

Diagnostic and Non-diagnostic Methods: Specific Examples

Diagnostic
A method of measuring the nitrogen monoxide content during exhalation requires the presence of the patient, hence it is considered to be a technical step practised on the human body. The other steps of the method - comparison with standard values, finding of a deviation, and attribution of the deviation to a clinical picture –were all held to be non-technical in nature, and so a claim like this is considered to be an unpatentable method of diagnosis.

Non-diagnostic
A method performed on the body which does not enable a medical condition to be identified, but which may be of value in diagnosis is not considered as method of diagnosis. Thus, a method of taking a sample, or determining internal temperature or pH, does not identify a condition and would be considered as a patentable subject matter in view of Section 22.3 of the IP Code.

A fitness test, wherein the general physical state of an individual is determined, is not considered to be diagnostic if it is not intended to identify or uncover a pathology.

Likewise, a method carried out by a device without implying any interaction with the human or animal body, for instance by using a specific software program, may not be considered to satisfy the criterion "practised on the human or animal body", because their performance does not necessitate the presence of the latter. By the same reasoning, this criterion is neither complied with in respect of method steps carried out in vitro in a laboratory.

5.2 Medical Use Claims
The exclusion in Sec. 22.3 applies only to methods of treatment and diagnosis and not to the products and compositions used in such methods, as explicitly stated. Thus, patents may be obtained for products and composition for use in these methods of treatment or diagnosis, particularly substances or compositions. This provision therefore explicitly allow patent protection for the medical use of a product or composition.

For the purpose of patent protection of a medical application of a substance, a claimed use to be considered an invention eligible for patent protection, needs to find a practical application in the form of a defined, real treatment of any pathological condition.

5.2.1 First medical Use
When a substance is known, but its pharmacological properties are not disclosed in the art, first medical use maybe claimed in the form of a purpose-related product claim. The technical teaching being the novel and inventive purpose of the known substance.

The MSEP discussed that medical use claims are exception from the general principle that product claims can only be obtained for (absolutely) novel products. These type of claims will be regarded as restricted to the substance or composition when presented or packaged for the specified use. First medical use must fulfill all other requirements of patentability, especially that of patent eligibility and inventive step.

A first medical use claim of the form "(substance X) for use in therapy" would be anticipated by any prior use of the substance in therapy. If any prior medical use is found, an amendment of the claim to the second medical use format is accepted.

Determination on iventive step will also be focused on the claimed use vis a vis any prior medical use in the art.

First medical use: Claim Format
The drafting of first medical indication patents may take the following forms:

i) Compound/composition X for use in therapy;
ii) Compound/composition X for use as a medicament;
iii) Compound/composition X for use in the treatment of medical condition Y

The broad form of first medical use claim is allowable for the first medical use of a substance or composition, providing there is support in the form of evidence for at least one medical use.

The Swiss type form of claim is also acceptable when claiming a first medical indication.

5.2.2 Second Medical Use Claims

In assessing applications with second medical use claims, it is important to understand how second medical use is presented within the context of the QUAMA provision.

If an application includes unpatentable method of treatment claims, such as the use of X to treat Y, amendment of these claims to convert them into second medical use claim format does not constitute added matter and thus accepted anytime during examination stage.

The examiner should note that for a therapeutic application to be construed as a further medical use, this new technical effect of a known substance must lead to a truly new therapeutic application, which is the treatment of a different pathology.

5.2.3 Second medical use: Claim format

Second medical uses are to be drafted in a Swiss-type claim format.[2] Claims relating to the use of a substance for the manufacture of a medicament are permitted where the novelty is derived from the new pharmaceutical use –not the product-since the product was old, even if the manufacturing procedure was not in itself novel and the active ingredient was known.

In a Swiss type claim, it is considered that the intended purpose of the manufacture of the agent was the use of a known compound in the treatment of the human or animal body by surgery or therapy or in a diagnostic method.

Swiss-type claims are drafted according to the following formats:

- ✓ Use of a substance X in the manufacture of a medicament for the treatment of disease Y.
- ✓ Method for manufacturing a medicament intended for therapeutic application Y, characterised in that substance X is used.
- ✓ Process for the manufacture of a medicament for the therapeutic application Y characterized in that substance X is used.

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[2]It is noted that the European Patent Office(EPO) has already abandoned this type of claim format in view of European Patent Convention 2000 (EPC 2000). However, the scope of this new claim format has not yet been tested. There are speculations that the scope of the new claim format is broader than the Swiss type. In this regard, the PH will continue to accept Swiss type claims for subsequent medical use claims. This claim format will also help the examiners distuinguish subsequent medical use claims over first medical uses.

These types of claims are construed as an activity of formulating the medicament's active substance which constituted the process for obtaining the medicament, which will pass the requirement of industrial applicability.

Second medical use: the new use
The examiner should be guided with the following discussion when deciding what constitutes a "new medical use"[3]. Claims would not be acceptable if they simply provide additional information about an old therapeutic application or treatment. Specifically, a second medical use must: a)provide for a therapeutic application; and b)indicates that the therapeutic application is new.

Medical use claims with the folllowing features do not qualify as valid second medical use claims for the reasons outlined hereunder.

- New mode, time, frequency or dosage of administration
  A second medical use claim which is distuinguished from the prior art by the dosage regime, or the mode of administration (for example, intramuscular vs. intravenous injection) shall be construed as methods of treatment, disguised by drafting in the subsequent medical use claim format. These claims define an improvement in the method of administering an existing treatment, it does not define a new therapeutic application, thus failing the requirement to be considered as new medical use. Moreover, these features are directed to the steps of a method of treatment.

- New patient group
  A second medical use claim distuinguished from the prior art solely by the new patient group do not qualify as a new therapeutic application. This kind of claim provides an information on additional advantage, hence do not constitute a new therapeutic application.

- New mechanism or technical effect
  Second medical use claims which relate to the newly found technical effect or mechanism of action of the same therapeutic use as the prior art shall be considered as inherent, see discussion in Case B. This type of claim only provides more information about the old use, i.e., how a treatment worked, hence do not qualify as new medical use.

- New advantage to known use
  The finding of a new advantage in a known treatment does not constitute a new therapeutic use. This is merely drawn to a new piece of information about a known treatment.

- New clinical situation
  The discovery of a new clinical situation (new strategy for therapy) for a known treatment does not constitute a new medical use. This feature of the claim provides additional advantage to the known medical treatment, hence do not constitute a new therapeutic use.

5.3 Evidence of Support in the Description
A claim to the first and medical use of a known substance or composition should be supported by evidence of its efficacy in therapy, surgery or diagnosis since the claims

[3]Before the enactment of RA 9502, there are similarities between PH and EPO practices in interpreting subsequent medical uses. The EPO has historically taken a more liberal view of what constitutes a "new medical use". In light of the QUAMA provisions, the PH cannot follow suit anymore.

are distinguished from the prior art by their use. This requirement is also applicable to second (further) medical use invention. The application as filed must provide clinical test, an animal experiment, or in vivo or in vitro data as evidence for support, and cannot be overcome by later-filed results. In the absence of any such evidence, the claim is considered as merely speculative and a support objection should always be made.

If the first or second (further) medical use claim is included as a subsidiary claim to a new and inventive substance or composition, further consideration of support for the medical use claim is not necessary.

An application filed in the Philippines which relates to unpatentable method of treatment claims when redrafted into second medical use claim format does not constitute added matter and thus accepted anytime during examination stage. However, the examiner shall exercise vigilance in assessing claims on method of treatment disguised as a second medical use.

6. BACKGROUND ON DOCTRINE OF INHERENCY AS APPLIED IN THIS QUAMA GUIDE

Since the concept of Doctrine of Inherency is adopted in qualifying what mere discoveries are within the purview of the QUAMA provisions, this subsection presents how the principles of inherency shall be applied in this QUAMA Guide.

The Doctrine of Inherency has been, most often, considered in other jurisdiction during the novelty/anticipation inquiry where inherent disclosure is embodied in a prior art document or prior use/sale/offer of sale. It has been occasionally used for establishing compliance with the written description and enablement requirements where embodied in the specification of a patent application. Recently, U.S. case laws have shown inherent disclosure being considered during obviousness inquiry.

In this QUAMA Guide, a new concept of applying the inherency principles is introduced. Specifically, said inherent disclosures are considered during patent eligibility criterion inquiry and in the assessment of inventive step requirement, where applicable. As regards inherent disclosure in the assessment of novelty, a new form or new use of known substance deemed inherent shall be considered not novel as well.

Generally, an inherent result is one that necessarily and inevitably flows from a particular action or operation. Examples of an action that produce an inherent result include: steps of a process or method, working example reciting the preparation of a substance, typical operation of machine, typical routine works of a person skilled in the art, among others.

On the same note, if a previously unknown advantage or benefit, necessarily and inevitably follows from the subject matter expressly disclosed in the prior art, i.e., if the advantage or benefit is inherent in what the prior art discloses, a later claim to said advantage or benefit is also deemed as inherent.

It has been known in patent literature that an inherent result can be readily recognized or hidden. A recognizable inherent result is said to be either apparent or scientifically inferable from the express disclosure, hence, generally easy to establish. On the other hand, a hidden inherent result would require an empirical evidence in order to be established, as this result is neither recognizable nor scientifically inferable from what is explicitly disclosed in the prior art. Moreover, hidden inherent result can be implicitly intended or totally accidental. A hidden result that is

necessary and inevitable link in producing an expressly intended or disclosed result is implicitly intended. An accidental result is a hidden inherent result that is unintended and unappreciated.

Inherent result, whether readily recognizable or hidden - implicitly intended or totally accidental shall be considered mere discoveries, hence non eligible for patent protection when later claimed. This concept also deviates from the understanding in other jurisdictions where accidental result are exceptions in inherency analyses.

Because inherency places subject matter in the public domain as well as an express disclosure, the inherent disclosure of the entire claimed subject matter anticipates as well as inherent disclosure of a single feature of the claimed subject matter. The extent of the inherent disclosure does not limit its anticipatory effect.

In general, a limitation or the entire invention is inherent and in the public domain if it is the "natural result flowing from" the explicit disclosure of the prior art."Inherency is not necessarily coterminous with knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art."

In applying the inherency principles when examining Cases A, B and C, reference should be made on the concept notes presented in each case. The concept note may be written as part of the substantive examination report to provide basis of the analysis made by the examiner.

As pointed in the introduction, the illustrations hereunder are merely explanatory, and to be used as reference, consistent with the general policy rationale in RA 8293 and with the principle in RA 9502. Each application must be examined on a case-by-case basis taking into consideration the facts of each case.

6.1 Doctrine of Inherency as applied during Non patentable Subject Matter Inquiry

In light of the principles and concept outlined above, it is important to be guided by the general direction of understanding as discussed below in order to arrive to a more definitive definition of mere discovery during patent eligibility inquiry.

6.1.1 Case A

Three cases are contemplated, namely:

i.) where a new form inevitably and necessarily flows from the explicit disclosures of the prior art
ii.) where a non-inherent new form does not impart any enhancement of the known efficacy,
iii.) where a non-inherent new form resulted to any enhancement of the known efficacy, but one which is an inherent result or inherent advantage/benefit

The three cases above shall be considered as "mere discoveries", hence, drawn to ineligible subject matter under Section 22.1, as amended by RA 9502.

6.1.2 Case B

A subsequent new use which necessarily and inevitably flows from the mechanism of action or any property expressly disclosed in the prior art, is inherent, and shall be deemed mere discovery, hence, shall be excluded from patent protection.

6.1.3 Case C

Where the claim is drawn to a similar process known in the art, such process shall be deemed as mere discovery and inherent unless a different product is produced and at least one reactant is employed.

6.2 Doctrine of Inherency as applied during Inventive Step assessment

If a QUAMA application passes the patent eligibility criterion, the same shall be subjected to inventive step assessment where the usual methodology and principles are applied, including Doctrine of Inherency principles, where applicable.

As discussed in the General Guidelines, while "enhanced efficacy" could render a new form of a known compound eligible for patent protection, the same does not demonstrate inventive step for an obvious new form because without the exercise of any inventive ingenuity, any additional advantage, even if unexpected, could only be considered as a gratis effect which would inevitably have resulted from the non-inventive activity. Thus, even though the new form resulted to unexpected enhanced efficacy, the same should still be rejected if the new form is found to be non-inventive in light of the prior art. On the same note, the claimed new use shall be deemed as obvious if the prior art provides a clear direction to motivate a person skilled in the art to employ such known substance for such new use.

B. EXAMINING CLAIMS DIRECTED TO NEW FORMS OF KNOWN SUBSTANCES (Case A)

This Section illustrates the application of inherency principles when examining claims which are drawn to new forms of known substances.

When a claim is supposed to qualify as Case A, the examiner should establish first that the substance by which the new form is appended to is already known in light of prior art documents. If said substance is indeed known, reference hereafter provides guidance during substantive examination.

7. Non patentable Subject Matter Inquiry

Reference is made to Figure 1 below when determining whether a QUAMA application that qualifies as Case A is patent eligible or not.

Step 1 is represented in diamond (1), and determines whether the claim is directed to a new form of known compound. If yes, proceed to Step 2. Consider each claim separately based on the particular elements recited therein. New forms of known substances may cover:

- isomers, stereoisomers, polymorphs, metabolites, prodrugs, homologues, hydrates, acid addition salts, pure forms, new particle size of known pharmaceutical compounds
- various derivatives of known chemical compounds such as esters, ethers, complexes and other derivatives thereof
- compositions or formulations comprising the known compound. These compositions or formulations may comprise excipients or pharmaceutically acceptable carriers such as binders, diluents or fillers, stabilizing agents, disintegrants, and lubricants.
- combinations of known substances, including kits
- Known substance refers to a known chemical compound or biological substance, other than food.

Step 2 is represented in diamond (2), and determines whether the new form is inherent, i.e. inevitably and necessarily flows from the explicit disclosures of the prior art. If yes, the claim is not an eligible subject matter under Section 22.1 as being drawn to non patentable subject matter using the Office Action standard template for QUAMA Case A. If no, proceed to Step 3.

Step 3 is represented in diamond (3), and determines whether the new form has resulted to the enhancement of the known efficacy of the known compound. If no, the claim is ineligible, and should be rejected under Section 22.1 as being drawn to non patentable subject matter using the Office Action standard template for QUAMA Case A. If yes, proceed to Step 4.

- Efficacy may refer to the “therapeutic efficacy” or to any of the “advantageous properties” (e.g. bioavailability, stability, solubility among others) exhibited by the new form of a known substance.
- Enhancement of efficacy may also refer to the improved or unexpected properties of known pharmaceutical substances such as increased bioavailability, lower neurotoxicity, higher potency, which are not found in the original pharmaceutical substance.
- Enhanced efficacy can also be proved by factors such as lesser side-effects, wider spectrum of activity, reduction in treatment time etc.

Step 4 is represented in diamond (4), and determines whether the enhancement is inherent using the guidance as discussed in this QUAMA Guide. If yes, then the claim is ineligible and should be rejected under Section 22.1 as being drawn to non patentable subject matter using the Office Action standard template for QUAMA Case A.

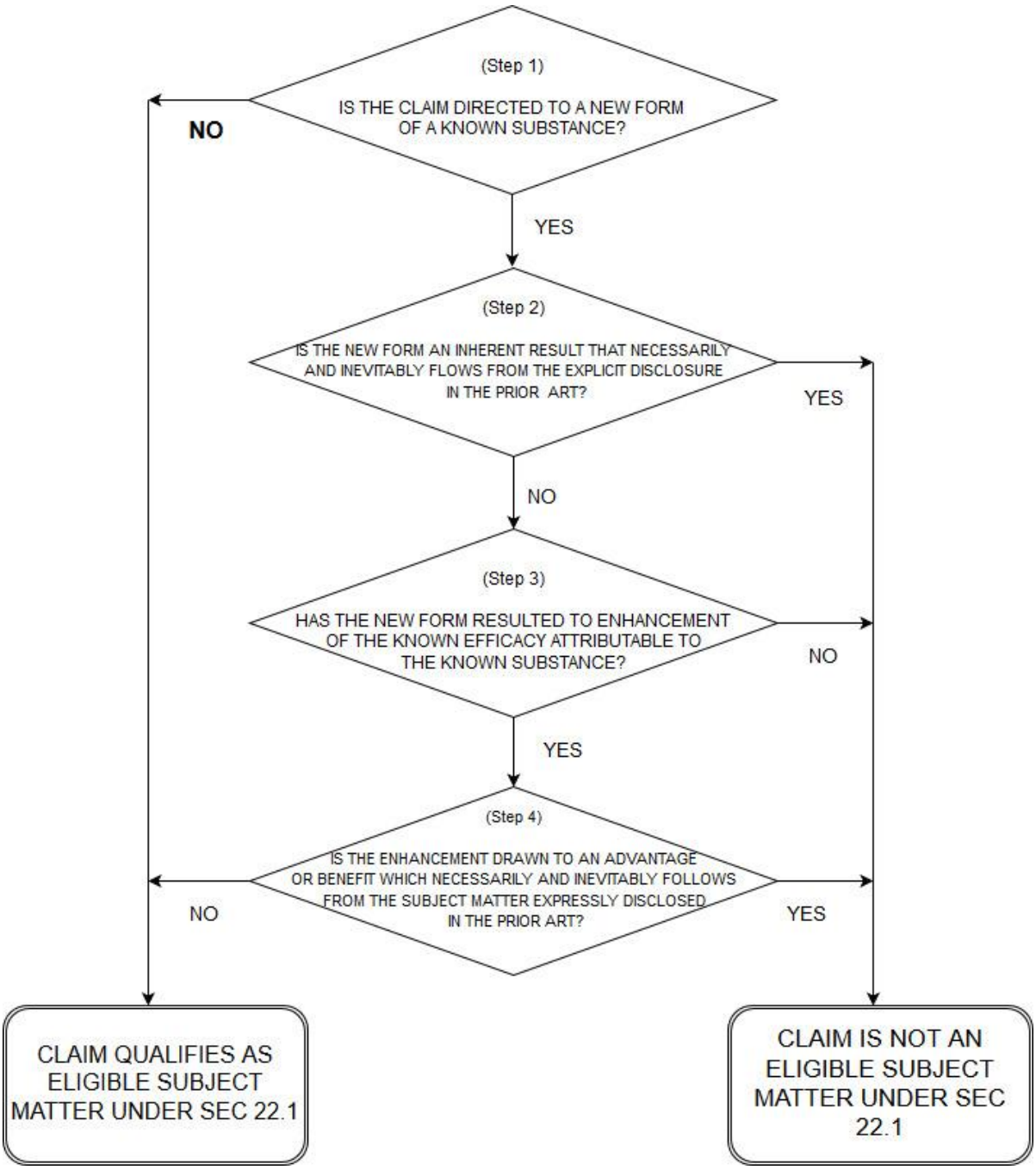

Figure 1. Flowchart for determining the patent eligibility of new forms of known substances under Section 22.1, as amended by RA 9502.

The above flowchart provides a summary of the guidance set out in this QUAMA Guide and it illustrates the subject matter eligibility analysis for claims relating to new forms of known compounds.

7.1 Illustrative Examples

Based on the guidance enunciated above, we can now turn to examples to illustrate how the guidance provided in this Section can be applied when examining claims directed to new forms of known substances.

<u>Concept 1</u> "**If the new form is an inherent result that necessarily and inevitably flows from the explicit disclosure of methods/process in the prior art, said new form is mere discovery.**"

Example 1

INVENTION : Hemihydrate form of Compound A

PRIOR ART : Method of manufacturing the anhydrous form of compound A that naturally results in the production of at least trace amounts of the hemihydrate form.

Overview of the Description: The description described the claimed hemihydrate form of which is more stable than the parent compound A.

COMMENT

Compound A being known, the claim is drawn to a new form of known substance. The flowchart for Case A provides the following rationale for the rejection based on inherency principles.

Step 1: Is the claim directed to new form of a known compound?
Yes

Step 2: Is the new form inherent?
Yes. The hemihydrate form of compound A is an inherent result that necessarily and inevitably flows from the explicit disclosure in the prior art because a small fraction of the anhydrous form spontaneously converted to the hemihydrate form during the production of the anhydrous form. Since the claims covered compounds that were the natural and necessary result of prior art process, notwithstanding that the art may not have recognized or appreciated the compounds, the claims are inherently disclosed.

Decision: Claim is drawn to mere discovery of new form of a known substance, hence ineligible for patent protection.
The hemihydrate form of compound C is held inherent when (a) producing the anhydrous form according to the prior art's process inevitably results in the production of at least trace amounts of the hemihydrate form, (b) it was undisputed that the first known existence of the hemihydrate form resulted from an attempt to produce the anhydrous form according to the process of prior art.

Example 2

INVENTION : Metabolite D of Compound C

PRIOR ART : A class of compounds called antihistamines, including compound C is already known. The administration of compound C to a patient is also taught. However, said reference does not expressly disclose metabolites of compound C and does not refer to metabolites of Compound C.

Overview of the Description: The metabolite D is also a non-drowsy antihistamine, like its parent compound C.

COMMENT

It is known to a person skilled in the art that a metabolite is the compound formed in the patient's body upon intake of a medicine. In this case, the ingested Compound C undergoes a chemical conversion in the human digestion process to form a new metabolite compound. Hence, the metabolite is a new form of a known compound,

rendering the claim as Case A. The flowchart provides the rationale for the decision on similar cases like this.

Step 1: Is the claim directed to new form of a known compound?
Yes

Step 2: Is the new form inherent?
Yes. A patient ingesting compound C would necessarily metabolize that compound to metabolite D. Hence, metabolite D is considered as inherent even though its existence was not known at the time the prior art is created because it is the "natural result flowing from" the explicit disclosure of administering the compound A to a patient.

Decision: Claim is drawn to mere discovery of new form of a known substance, hence ineligible for patent protection
It is not required that a skilled artisan has to recognize the inherent characteristic in the prior art to establish inherency when (a) metabolite D is a necessary consequence of administering compound C to patients i.e. is not formed accidentally or under unusual conditions when compound C is ingested and (b) necessarily and inevitably forms from compound C under normal conditions.

Example 2, where the inherent result of the body's production of metabolite D was not readily recognized and it was unintended, is an example of an accidental result. Nevertheless, metabolite D shall still be considered as mere discovery within the purview of the QUAMA provision.

Example 3

INVENTION : R(+) of Compound E useful in the treatment of pain, where side effects are eliminated.

PRIOR ART : Compound E, in racemic mixture, belong to NSAIDS. Its molecular structure shows a chiral carbon. There were no disclosure on the stereoisomers. Separation techniques are known in the art.

Overview of the Description: Administering Compound E in a patient causes some side effects. It was found that the R(+) isomer of Compound E had much higher activity than the other isomer. Separation process follows conventional methods known in the art.

COMMENT
An isomer is a new form of the known Compound E. Hence, the flowchart for Case A applies here.

Step 1: Is the claim directed to new form of a known compound?
Yes

Step 2: Is the new form inherent?
Yes. An isolated enantiomer is inherently disclosed in the racemic mixture of Compound E, as the presence of a chiral carbon necessarily discloses the existence of both enantiomers. It is known in organic chemistry that enantiomers inevitably occur in compounds that comprise a chiral carbon atom. The process of isolating the enantiomer is based on ordinary methods known in the art.

Decision: Claim is drawn to mere discovery of new form of a known substance, hence ineligible for patent protection.
It is known for a person skilled in the art that the pharmacological/therapeutic effect of a racemic mixture is almost entirely or entirely based on the active enantiomer. Hence, an individual

enantiomer, although resulted to enhancement of the known efficacy, is still ineligible for patent protection under Section 22.1 for being drawn to a mere discovery of new form of known substances.

Generally, once a racemic compound is known, finding which of the enantiomers has the pharmacological/therapeutic activity shall be deemed mere discovery because a person skilled in the art knows that a compound having a chiral center exists in two optically active forms.

Example 4

INVENTION: A substantially pure (+)-enantiomer of compound F and non-toxic acid addition salts thereof, which is a selective serotonin reuptake inhibitor (SSRI) used in the treatment of depression.

PRIOR ART: A racemic mixture of compound F and descriptions of techniques available to separate enantiomers from their racemates. However, the difficulty of separating enantiomers and the unpredictability of their properties are not known.

COMMENT

This case may likely be rejected as patent ineligible, being drawn to a mere discovery of new form. Rejection on patent eligibility of compound F based on inherency analysis may be rebutted by the evidence demonstrating the difficulty of separating the enantiomers and the unexpected properties of the (+)-enantiomer of compound F. The substantially pure (+)-enantiomer of compound F may be considered not a mere discovery when the known difficulty of separating enantiomers and the unpredictability of their properties are not disclosed in the prior art.

Concept 2 "**If a previously unknown advantage or benefit necessarily and inevitably follows from the subject matter expressly disclosed in the prior art, a later claim to said advantage or benefit is also deemed as inherent.**"

Example 5 New form of a compound exhibiting properties which are attributable to polymorphism

INVENTION : Beta crystalline from of methane sulfonic acid addition salt of Compound G (parent compound) and processes for the preparation thereof. The substance claimed is used for the treatment of chronic myeloid leukemia.

PRIOR ART : The prior art described Compound G, its pharmacological properties are also known, including its use in the treatment of chronic myeloid leukemia. The prior art only described how to prepare Compound G in free base form. There was no mention of polymorphism or crystalline structure.

Overview of the Description: The description as filed asserted that the β-form has more beneficial flow properties, better thermodynamic stability and has lower hygroscopicity than the alpha crystal form of Compound G. However, there is no data to support an enhanced solubility or bioavailability, or any other advantages other than improved physical properties.

COMMENT

Since Compound G was already a known, the β-form is regarded as a new form of a known substance, hence qualifying as Case A. Reference to the flowchart provided in Figure 1 reveals the following findings:

Step 1: Is the claim directed to new form of a known compound?
Yes

Step 2: Is the new form inherent?
No. The β-form is not necessarily and inevitably obtainable following the process of producing Compound G. In fact, the prior art only described the preparation of the free base form of Compound G and there were no explicit disclosure would take a person skilled in the art to produce the β-form since polymorphism or any crystalline structure of Compound G was not mentioned at all.

Step 3: Has the new form resulted to enhancement of known efficacy?
Yes. The β-form was claimed to have more beneficial physical properties than the parent compound.

Step 4: Is the enhancement inherent?
Yes. It is inherent to a polymorph of a known compound to exhibit better thermodynamic stability and lower hygroscopicity.
Other than the enhanced physical properties which are typical to a polymorph, there are no additional enhancement of the known efficacy of Compound G provided in the description as filed.

Decision: Claim is drawn to mere discovery of new form of a known substance, hence ineligible for patent protection.

In this case, the enhancement of efficacy, which pertains to better thermodynamic stability and lower hygroscopicity properties, necessarily and inevitably follows from the known properties attributable to a polymorph. Hence, a claim to said advantage or benefit is deemed as inherent and could not render patentability to the claimed polymorph.

Example 6 A combination of a known compound causing a side effect and a second known compound recognized to suppress such side effect

INVENTION : A composition comprising compound H in combination with an effective amount of the compound I wherein vomiting caused by the administration of compound H is suppressed.

PRIOR ART : Compound H, while being a remarkable antitumor agent, causes vomiting as a side effect upon its administration. Compound H has been combined with secondary components other than compound I to suppress vomiting. Compound I, on other hand, is generally well known to suppress vomiting. In addition, the effect of compound I in the claimed combination falls within the extent predictable to a person skilled in the art.

Overview of the Description: It has been found that when compound H is used in combination with the compound I, tumors can be treated with the side effect of vomiting associated with compound H, is suppressed. The description provided the results of pharmacological study supporting the suppressed side effect.

COMMENT:
Compound H is known to be used in combination with a secondary component to suppress its side effect of vomiting. Compound I is also generally well known as a component to suppress vomiting. Hence, the new form is drawn to the combination of the two known compounds.

Step 1: Is the claim directed to new form of a known compound?
Yes

Step 2: Is the new form inherent?

No. Although each of the components are already known, their combination has not been disclosed and that the combination is not an inevitable and not a necessary result of performing methods explicitly mentioned in the prior art.

Step 3: Has the new form resulted to enhancement of known efficacy?
Yes. The combination suppressed the side effect associated with compound H.

Step 4: Is the enhancement inherent?
Yes. It would be an inherent result for the claimed combination of compound H to have a suppressed side effect of vomiting since compound I is generally known to suppress vomiting.

Decision: Claim is drawn to mere discovery of new form of a known substance, hence ineligible for patent protection.

The mere aggregation of the properties resulting from the mere admixture of known components and which does not result to unexpected synergism is inherent. In the present case, to reduce a side effect by optimizing the combination of the two components, the enhancement of known efficacy attributable to the combination of compound H and compound I shall be considered as an inherent result flowing from the known therapeutic effects of the two components.

Example 7

INVENTION : A therapeutic agent for AIDS characterized by comprising a combination of azidothymidine (AZT), which is an anti-HIV agent, and a compound J.

PRIOR ART: Azidothymidine (AZT) is known to be an effective therapeutic agent for AIDS. It is also known that pneumonia is one of the various symptoms caused by HIV. Moreover, the compound J is commonly used to treat pneumonia.

Overview of the description: In this invention, it has been shown that, in order to treat AIDS that develops following the HIV infection, the use of the combination of an anti-HIV agent AZT, and the compound J, which is effective to treat pneumonia developed as an aspect of AIDS, is effective in suppressing the progress of HIV and in treating pneumonia.

COMMENT:
The claim is drawn to combination of known compounds. Reference to the flowchart for Case A provides the rationale for the inherency analysis.

Step 1: Is the claim directed to new form of a known compound?
Yes

Step 2: Is the new form inherent?
No. Although each of the components are already known, their combination has not been disclosed and that the combination is not an inevitable and not a necessary result of performing methods explicitly mentioned in the prior art.

Step 3: Has the new form resulted to enhancement of known efficacy?
Yes. The combination, while being effective in suppressing the progress of HIV, is also effective in treating pneumonia.

Step 4: Is the enhancement inherent?
Yes. In light of the known therapeutic effect of anti-HIV AZT and compound J, it would be an inherent result for the claimed combination of these components to treat pneumonia developed as an aspect of AIDS, while suppressing the growth of HIV, which is the cause of AIDS.

Decision: Claim is drawn to mere discovery of new form of a known substance, hence ineligible for patent protection.

As discussed above, without unexpected synergism, the mere aggregation of the properties resulting from the mere admixture of known components is inherent. In the present case, the use of the combination of an anti-HIV agent AZT and the compound J, for the purpose of treating pneumonia developed as an aspect of AIDS, while suppressing the growth of HIV, which is the cause of AIDS, has not provided a synergism which could not be predicted by a person skilled in the art, hence, shall be considered as an inherent result flowing from the known therapeutic effects of the two components.

Concept 3 "**An enhancement of efficacy attributable to the new form of a known substance that is surprising and unexpected, and which do not necessarily and inevitable flows from the teachings of the prior art are not inherent.**"

Example 8 A combination showing synergistic effect

INVENTION: A composition comprising a compound K and a compound L in a specific ratio of 5:1 to 4:1 by weight. The composition is useful in the treatment of diabetes and side effects are reduced.

PRIOR ART: Each of the compound K and the compound L is used to treat diabetes. However, no prior art document describes the combination of compound K and the compound L. The state of the art shows that a person skilled in the art could not predict the reduced side effects such as body weight when the claimed composition is administered to a diabetic person.

Overview of the description: It has been found that the combination of the compound K and the compound L in a specific ratio resulted to a reduction of body weight gain, a side effect when compound K is taken alone.

The description as filed provided a data of the pharmacological study showing the use of the combination of the compound K and the compound L in a specific ratio provides the reduction of the side effects.

COMMENT:
Since Compounds K and L are already known for the same therapeutic use, the claimed combination is a new form of known compounds. Thus, the flowchart for Case A applies here.

Step 1: Is the claim directed to new form of a known compound?
Yes

Step 2: Is the new form inherent?
No. Although each of the compound are being used in the treatment of diabetes, the combination is not an inevitable and not a necessary result of performing methods explicitly mentioned in the prior art. Not to mention that the specific ratio has not been disclosed in the prior art.

Step 3: Has the new form resulted to enhancement of known efficacy?
Yes. The composition provided a reduction of the side effects attributable to Compound K when taken alone.

Step 4: Is the enhancement inherent?
No. The synergy of the two compounds is not an accidental result nor implicitly intended result from the explicit disclosures of the prior art. A person skilled in the art could not predict, at the time of filing, that a

reduction in body weight gain is attained when the combination is used to treat diabetes.

Decision: Claim is drawn to a patent eligible subject matter. Proceed to examination of novelty and inventive step accordingly.

8. Novelty

If the claims related to new forms pass the patent eligibility test in view of inherency principles, the same are to be subjected to novelty assessment based on the explicit disclosures in the prior art. When the claims are deemed to be discovery, the subject matter sought for protection should be rejected as lacking novelty as well.

9. Inventive Step

In support to inventive step, the applicant should demonstrate that the new form of a known substance exhibits an "unexpected" or "improved" result, which would then provide for the enhancement of the known efficacy.

For purposes of establishing that a new form or a new property differs significantly with regard to efficacy as compared with the known substance, a patent applicant must provide data comparing the efficacy of the new form with that of a known substance.

A reasonable correlation between the efficacy claimed and the data provided shall be demonstrated and substantiated by relevant data documenting the activity of the new form, relevant results of experimental assays (*in vivo* and/or *in vitro*), other pre-clinical or clinical test data, or any combination thereof.

Due to the advanced technology in all fields of science, it is possible to show by giving necessary comparative details based on such science that the new form of a known substance had resulted in the enhancement of the known efficacy of the original substance.

Efficacy, however, need not be quantified in terms of numerical value to determine whether a product is efficacious because it is not possible to have a standard numerical value for efficacy for all pharmaceutical products.

The reference point for any comparison with regard to properties or enhancement of efficacy should be the filing date of the application or the relevant priority date, if the application is claiming the priority of any earlier application, but not at the stage of subsequent development. This is because a patent is granted on the basis of its full disclosure of the invention in the description furnished on the priority date of the application.

When assessing the extent of enhancement of efficacy, the patent examiner may call on representatives of the Food and Drug Administration (FDA), formerly the Bureau of Food and Drugs (BFAD), and/or its delegated experts to provide an expert opinion with regard to significant enhancement of therapeutic efficacy. Such expert opinion, however, is not binding but serves only as guide in the determination of inventive step in relation to the efficacy of a drug or medicine.

9.1 Illustrative Examples

The following examples illustrate how the guidance in this Section can be applied in practice, during assessment of inventive step of a QUAMA A deemed as patent eligible subject matter.

<u>Concept 4</u> "Patentability is not imparted where the synergy have resulted from an obvious new form of a known substance. Without the exercise of any inventive ingenuity, any additional advantage, even if unexpected, could only be considered as a gratis effect which would inevitably have resulted from the non-inventive activity"

Example 9

INVENTION: A synergistic combination of Compound M, or a pharmaceutically acceptable salt thereof and Compound N, or a pharmaceutically acceptable salt thereof.

PRIOR ART: Compound M is a remarkable antiretroviral drug from the protease inhibitor class used to treat HIV and AIDS. Compound N has been shown to be a potent secondary protease inhibitor. Specifically, Compound N has been shown to exhibit a booster effect for Compound X. The mechanism behind the booster effect is not known. In addition, HIV protease inhibitors are known to be metabolized by cytochrome P450 monooxygenase, a liver enzyme.

Overview of the Description: The inventors found out that Compound N actually inhibits a liver enzyme-ctyochrome P450 which metabolizes protease inhibitors. The bioavailability of Compound M is twice the value it had when administered alone. The combination is superior in terms of potency and shown to be a beneficial treatment as shown in the pharmacological data provided in the description as filed.

COMMENT:
Following the guidance set out in Figure 1, the claimed combination is drawn to a patent eligible subject matter.

Step 1: Is the claim directed to new form of a known compound?
Yes

Step 2: Is the new form inherent?
No. Although each of the compound are being used in the treatment of HIV and AIDS, the combination is not an inevitable and not a necessary result of performing methods explicitly mentioned in the prior art.

Step 3: Has the new form resulted to enhancement of known efficacy?
Yes. The composition provided a synergism which could not be predicted by a person skilled in the art.

Step 4: Is the enhancement inherent?
No. The synergy of the two compounds is not an accidental result nor implicitly intended result from the explicit disclosures of the prior art. A person skilled in the art could not predict, at the time of filing, that a superior potency is attained when the combination is used to treat HIV and AIDS since the mechanism of the booster effect of Compound N was not yet known at the time of the claimed invention.

The claim is deemed to be not inherent and novel as the combination is not disclosed in the prior art. The enhancement of efficacy, which in this case is the unexpected superior potency, should be assessed whether it could demonstrate inventive step.

Following the Problem Solution Approach, the closest prior art is taken to be the document disclosing the combination of Compound N with Compound X. The technical problem is seen to be the provision of an alternative HIV drug which is superior in potency. Based on the disclosure in the prior art, the booster effect of Compound N has already been shown with Compound X, another protease inhibitor.

Even though the mechanism or scientific principle behind the booster effect of Compound N is not yet known at the time the claimed invention was filed, a person skilled in the art would be motivated to look for other combinations comprising Compound N, with the expectation of success, in order to arrive at the claimed combination. Such endeavor falls within the normal routine work within his ordinary skill and common sense. Hence, the claimed combination, although offers an unexpected superior enhanced efficacy, should still be deemed obvious.

<u>Concept 5</u> "Patentability is imparted where the enhancement of efficacy could not be predicted by a person skilled in the art in light of the teachings of prior art".

Example 10

INVENTION: Synergistic combination of compound O and compound P useful as antibacterial with no toxic side effects

PRIOR ART: Compound O, which is a broad antibacterial spectrum of quinolones, and Compound P, a nitroimidazole are known compounds. Monotherapy with both compounds caused mild to moderate hepatoxicity and nephrotoxicity. Both drugs have similar pharmacokinetic profile with long half-lives suitable for parenteral administration An undue experimentation and inventive skill would require a person skilled in the art to combine said compounds based on his common knowledge.

Overview of Description: Compound O, was discovered by the inventors to have a very high gram-negative activity, including moderate activity against Pseudomonas aeruginosa while most anaerobic pathogens and several gram-positive strains are moderately susceptible to it. Compound P, a nitroimidazole, has an antibacterial spectrum that includes most of anaerobes. To increase the spectrum and to lessen the chances of resistance, it was combined with Compound O, a nitroimidazole which has an antibacterial spectrum that includes most of anaerobes. The additive advantage over monotherapy is that both drugs act on DNA and provide sequential block on bacterial DNA to contribute to synergistic activity. Compound P showed antioxidant potential and offers no obvious toxicity as compared to individual treatment. Pharmacological data is provided in the description as filed.

COMMENT:
A fixed dose combination of compound O and compound P could be considered to involve inventive step if the combination is superior in terms of potency and spectrum and shown to be a beneficial treatment than individual therapy of said drugs. Each of the components enhances the therapeutic effect of each other, an enhancement which could not be predicted by a person skilled in the art in light of the prior art documents.

Example 11

INVENTION: An extended release pharmaceutical composition comprising compound R (a derivative of the known compound Q) and a pharmaceutically acceptable polymer, for reducing gastrointestinal side-effects, whereby after ingestion certain specified parameters (pK limitations) of drug bioavailability are met.

PRIOR ART: A combination of references that disclosed
(a) extended release formulations of compound Q;

(b) extended release formulations of compound S (another derivative of the known compound Q) and their pK profiles; and
(c) extended release of a drug including compound R as an alginate salt.

COMMENT:
An extended release formulation of the antibiotic drug compound R, which aims to extend the period of drug effectiveness after ingestion and thereby reduce the requisite frequency of dosage, is considered to involve inventive step when the claimed pK limitations were not disclosed in any of the prior art as well as that there was no motivation for a skilled person to combine the teachings of the prior art references and come up with a reasonable expectation of success, i.e. a skilled artisan would not have predicted which formulation, that might be selected from the prior art, would provide the required pharmacokinetics; also, when there are dissimilarities in the pharmacokinetic properties and that the bioavailability of the formulations in the invention are not predictable from the prior art.

That when the problem is known, the possible approaches to solving the problem are known and finite, and the solution is predictable through use of a known option, then the pursuit of the known option may be obvious even absent a "teaching, suggestion, or motivation" concerning that option. Then, if this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Concept 6 **"Patentability is imparted where the prior art would not have suggested to a person skilled in the art that the process would have a *reasonable* likelihood of success and the resulting properties are unexpected."**

Example 12
INVENTION: A substantially pure (+)-enantiomer of compound F and non-toxic acid addition salts thereof, which is a selective serotonin reuptake inhibitor (SSRI) used in the treatment of depression.

PRIOR ART: A racemic mixture of compound F and descriptions of techniques available to separate enantiomers from their racemates. The difficulty of separating enantiomers and the unpredictability of their properties are not known.

COMMENT
As discussed in Example 4, the substantially pure (+)-enantiomer of compound F may not be considered a mere discovery when the known difficulty of separating enantiomers and the unpredictability of their properties are not disclosed in the prior art. It may be deemed inventive when the enhancement of efficacy is shown to be unexpected. In this case, where the therapeutic properties of the compound F would reside in its (+)-enantiomer resulting in having twice the potency of the racemic compound, the enhancement of efficacy cannot be foreseen by a person skilled in the art.

Lastly, that the prior art would not have provided the skilled person with a reasonable expectation of success at separating the enantiomers of the compound F when the difficulty involved in the separation would have motivated the skilled person to develop new compounds or divert his attention to another research of interest.

C. EXAMINING CLAIMS DIRECTED TO NEW USE OF KNOWN SUBSTANCES(Case B)

This Section illustrates the application of inherency principles when examining claims which are drawn to new use of known substances.

When a claim is supposed to qualify as Case B, the examiner should establish first that the substance by which the new use is appended to is already known in the prior art. If said substance is indeed known, reference hereafter provides guidance during substantive examination.

In general, if the new use is an inherent result that necessarily and inevitably flows from the explicit disclosure of methods/process in the prior art, said new use is a mere discovery.

Notwithstanding that the prior art may not have recognized or appreciated the use, the claims are inherently disclosed if it is a natural and necessary result of prior art process or methods. A new use is inherent if it is a necessary consequence of the methods or processes already known to a person skilled in the art.

On a similar note, a new use directed to an advantage or benefit, which necessarily and inevitably follows from the subject matter expressly disclosed in the prior art shall be deemed as mere discovery, being drawn to an inherent disclosure in the prior art.

10. Patent Eligibility

Reference is made to Figure 2 below when determining whether a QUAMA application that qualifies as Case B is patent eligible or not.

Step 1 is represented in diamond (1), and determines whether the claim is directed to a new use of known substance. If yes, proceed to Step 2.

- Consider each claim separately based on the particular elements recited therein.
- Known substance refers to a known chemical compound or biological substance, other than food
- The subsequent Steps in the flowchart serves as the guidance in determining whether the new use is a mere discovery using inherency principles.

Step 2 is represented in diamond (2), and determines whether the new use is inherent, i.e. , the new use is a newly found working mechanism of the known medical use. If yes, the claim is a mere discovery, hence, not an eligible subject matter. If no, proceed to Step 3.

Step 3 is represented in diamond (3), and determines whether the new use is inherent, i.e., the new use is conceived from the known working mechanism of the known substance. If yes, the claim is a mere discovery, thus ineligible for patent protection. If no, proceed to Step 4.

Step 4 is represented in diamond (4), and determines whether the new use is inherent, i.e., the new use is directed to a more specific concept of the known medical use. If yes, the claim is mere discovery, hence could not be given patent protection. If no, proceed to Step 5.

Step 5 is represented in diamond (5), and determines whether the new use is inherent, i.e., the new use has inevitably resulted from closely related pharmacological effects of the known substance. If yes, the claim is mere discovery, hence should be rejected. If no, proceed to novelty and inventive step assessment.

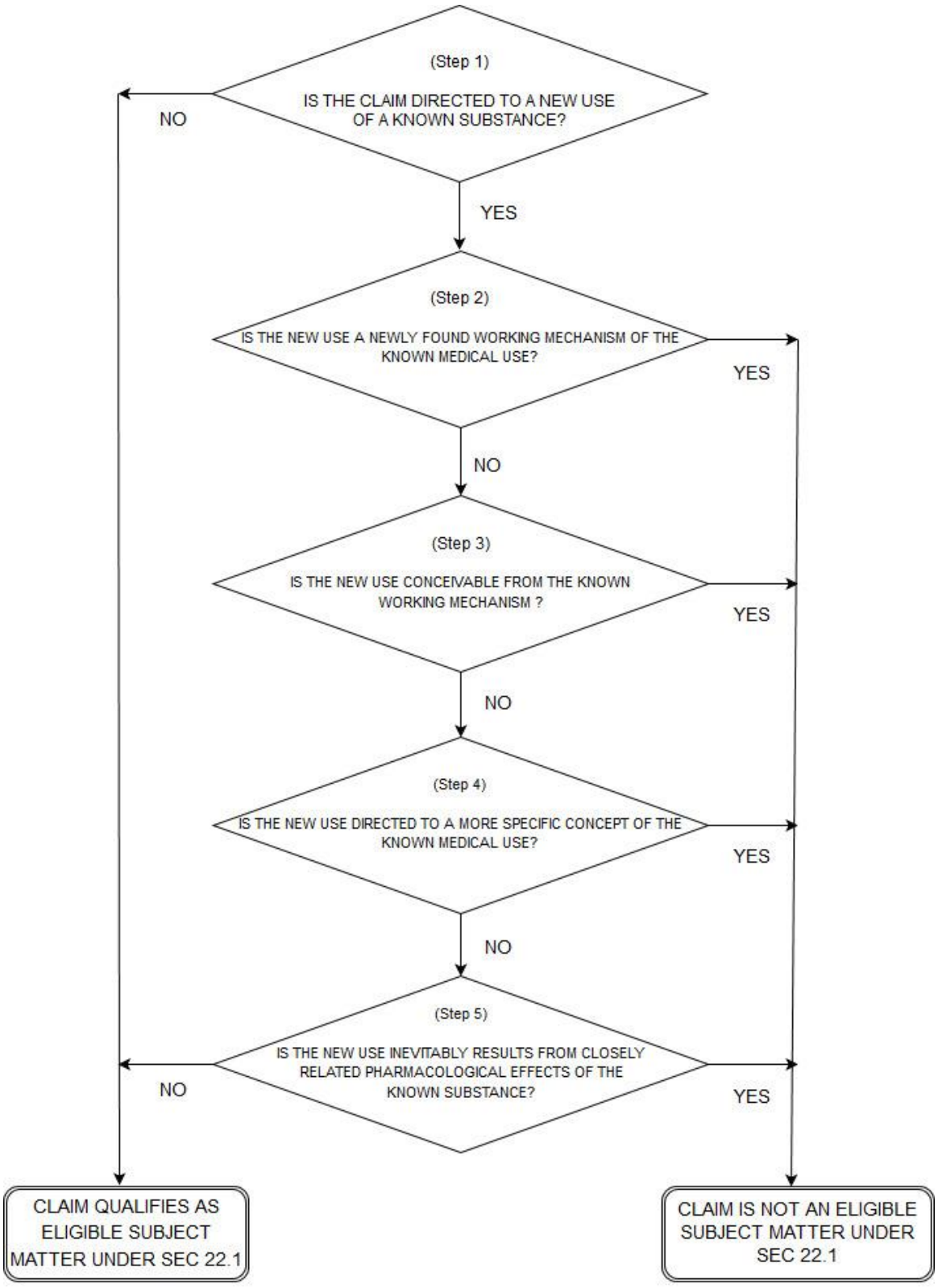

Figure 2. Flowchart for determining the patent eligibility of new use of known substances under Section 22.1, as amended by RA 9502.

10.1. Illustrative Examples

To illustrate how the guidance provided in this Section can be applied into practice, reference to hereunder examples should be made when examining claims directed to new uses of known substances.

Concept 7 "**A newly found working mechanism of the known medical use of the known substance is inherent**"

Example 13

INVENTION: The use of Compound X as Bacterial cell membrane formation inhibitor
PRIOR ART: Compound X as antibacterial agent

COMMENT
When the claimed medical use is only a newly found working mechanism of the known medical use of the known substance, and both uses cannot be substantially distinguished from each other, said claimed use is inherent.

Example 14

INVENTION: Use of a NO-synthetase inhibitor in the manufacture of a medicament for the treatment of diseases mediated by the kappa receptor Kk.
PRIOR ART: Compound S has been used in the treatment of cystic fibrosis

COMMENT
Cystic fibrosis is known to imply the involvement of said kappa receptor kK. The claim is inherent because the claimed therapeutic use encompasses cystic fibrosis, which is already known to be treated by compound X.

Concept 8 " **A new medical use conceivable from the known working mechanism of a known substance is inherent**"

Example 15

INVENTION: Use of compound X for the manufacture of a medicament for the treatment of anxiety.

PRIOR ART: Use of a compound X for the manufacture of a medicament for the treatment of diseases mediated by the 5-HTa receptor.

COMMENT
Anxiety is known to imply the involvement of 5-Hta receptor. The claim is inherent because the claimed therapeutic use is already encompassed by the known working mechanism.

Concept 8a " **A new medical use drawn to a more specific concept of the known medical use is inherent**"

Example 16

INVENTION: Use of compound Y for the manufacture of a medicament for the treatment of lung cancer.

PRIOR ART: Compound Y as anticancer agent.

COMMENT
Lung cancer is more specific concept of the known medical use of Compound Y as anticancer agent.

Concept 8b **"A representative disease falling within the known working mechanism of a known substance is considered as inherent"**

Example 17

INVENTION: Compound A for use in the treatment of erectile dysfunction
PRIOR ART: Compound A as cGMP-specific phosphodiesterase type 5(PDE5) inhibitor

INVENTION: Compound A as anti-pulmonary asthma
PRIOR ART: Compound A as bronchodilator

INVENTION: Compound B as hypotensive agent
PRIOR ART: Compound B as vasodilator

INVENTION: Compound C as therapeutic agent for angina
PRIOR ART: Compound C as coronary vessel dilator

INVENTION: Compound D as anti-allergy
PRIOR ART: Compound Das histamine liberation inhibitor

INVENTION: Compound E as agent for gastric ulcer
PRIOR ART: Compound E as histamine H-2 receptor inhibitor

Concept 9 **" A new medical use which has resulted from closely related pharmacological effects of the known substance is inherent"**

Example 18
CLAIM: The use of compound Z in the manufacture of a medicament for the treatment of pain.

PRIOR ART: Compound Z as anti-inflammatory

Example 19
The following table shows an example of cases and their patent eligibility under this Section.

Case	Claim	Prior Art	Patent eligible?	Basis
I	1. Product X for use as a medicament 2. Product X according to claim 1 for use in the treatment of asthma	X known as e.g. herbicide and no prior art that discloses any therapeutic activity of X	Yes, as first medical use (even if X is a known product, but its use in medicine is not known)	Sec 22.3, proviso part
II	The use of Product X for the manufacture of a medicament for the treatment of cancer	Case I	Yes, as second medical use (inventive step over Case I and any other prior art should be carefully scrutinized)	Sec 22.3, proviso part

III	The use of Product X for the manufacture of a medicament for the treatment of leukemia	Cases II and III	No (because leukemia is a specific type of cancer and considered as inherent in case II)	Sec. 22.1, as amended by RA 9502

11. Novelty

If the claims related to new use pass the patent eligibility test in view of inherency principles, the same are to be subjected to novelty assessment based on the explicit disclosures in the prior art. When the claims are deemed to be discovery, the subject matter sought for protection should be rejected as lacking novelty as well.

12. Inventive Step

Where the known substance has been used to treat a related condition, then inventive step of the the claim should be assessed carefully taking into account the merits of each application. If the diseases have a common origin, causative factors or mechanism, the claim may lack inventive step.

12.1. Illustrative Examples

The examiner may refer to the following illustrative cases during inventive step assessment of second(further) medical uses of known substances.

Concept 10 "**If the manifestations of the second more serious disease are known to run through the manifestations of the first disease, and this assumption reliably substantiated was not confuted, then the activity of a medicament against the more serious disease would already strongly suggest an effect also against the less serious one**"

Example 20

INVENTION: The use of prenyl ketone compound of formula (I) ……. for the preparation of a medicament for the treatment or prophylaxis of inflammation of the gastric mucosa

PRIOR ART:(a) The anti-ulcer effect of the prenyl ketone of the claim, i.e. geranylgeranylacetone (GGA), on experimentally induced gastric and duodenal ulcers in rats was disclosed

(b) The protecting effect of GGA against ulcer and to its protection against gastric mucosal damage in general induced by acetylsalicylic acid was also known. It was also disclosed that gastritis and ulcer are considered as distinct diseases characterized by different pathology.

Overview of the Description: The technical problem to be solved in relation to the prior art is to extend the field of therapeutic application of the prenyl ketone and that the solution proposed by the application is the use for the preparation of a medicament for the treatment of gastritis.

COMMENT

It is known that certain drugs such as aspirin and other non-steroidal anti-inflammatory drugs predispose to formation of an ulcer. It is also known that aspirin or other anti-inflammatory agents can generate gastritis.

Though gastritis and ulcer are distinct diseases, they have common aspects in relation to their "causative factors". Thus, the skilled person would expect that the cytoprotective activity of GGA applies to any kind attack by a mucous breaker aggressive agent such as acetylsalicylic acid, regardless of whether it eventually leads to gastritis or ulcer.

Concept 11 "**Without the exercise of any inventive ingenuity, any additional advantage, even if unexpected, could only be considered as a gratis effect which would inevitably have resulted from the non-inventive activity**"

Example 21

INVENTION: Second medical use of the Compound A directed to the treatment of erectile dysfunction in a male animal. Compound A is a potent and selective inhibitors of guanosine 3,5-monophosphate PDEs, more specifically PDEv.

PRIOR ART: (a) Compound B, which enhances the relaxation of the muscle responsible for causing an erection. Compound B is disclosed in the documents as a cGMP PDE inhibitor

(b) Compound B as PDE_V inhibitor, which causes relaxation in strips of human corpus cavernosum. Therapeutic activities could include treatment of impotence. It is also known in the art that zaprinast is a weak and non-selective PDE_V inhibitor.

COMMENT

There is a clear disclosure in the prior art: (i) that use of PDE_v inhibitors elevate cGMP, but not cAMP levels; (ii) that smooth muscle relaxation appears to be the most promising of the potential uses of PDE_v inhibitors; (iii) possible uses of PDE_v include, amongst others, the treatment of impotence; (iv) a clearer picture will be obtained when other rationally designed inhibitors become available.

The prior art explicitly provided the way forward. PDE_v inhibitors were said to be potentially useful for the treatment of MED and that a clearer picture would be obtained when inhibitors, other than the three mentioned, became available. Hence, the invention is obvious from the disclosure of the prior art.

Without the exercise of any inventive ingenuity, any additional advantage, even if unexpected, could only be considered as a gratis effect which would inevitably have resulted from the non-inventive activity. There could be no invention in doing what was suggested.

D. EXAMINING CLAIMS DIRECTED TO MERE USE OF KNOWN PROCESS(Case C)

This Section will guide the examiner in determining whether a claim directed to a new process is inherent, i.e. a mere use of known process which does not produce a new product and at least employ a new reactant, thus non patentable under the QUAMA provision.

13. Patent eligibility

Reference is made to Figure 3 below when determining whether a QUAMA application that qualifies as Case C is patent eligible or not.

Step 1 is represented in diamond (1), and determines whether the claim is directed to a known process. If yes, proceed to Step 2.

- Consider each claim separately based on the particular elements recited therein.
- Known process refers to a method or process comprising active steps in producing a certain substance

Step 2 is represented in diamond (2), and determines whether the known process has resulted to a new product. If no, the claim is a mere discovery, hence, not an eligible subject matter. If yes, proceed to Step 3.

- Case C, in order to become patentable, must also satisfy the requirement as set out in step 3.

Step 3 is represented in diamond (3), and determines whether the known process employed at least one new reactant. If no, the claim is a mere discovery, thus ineligible for patent protection. If yes, the claim is an eligible subject matter.

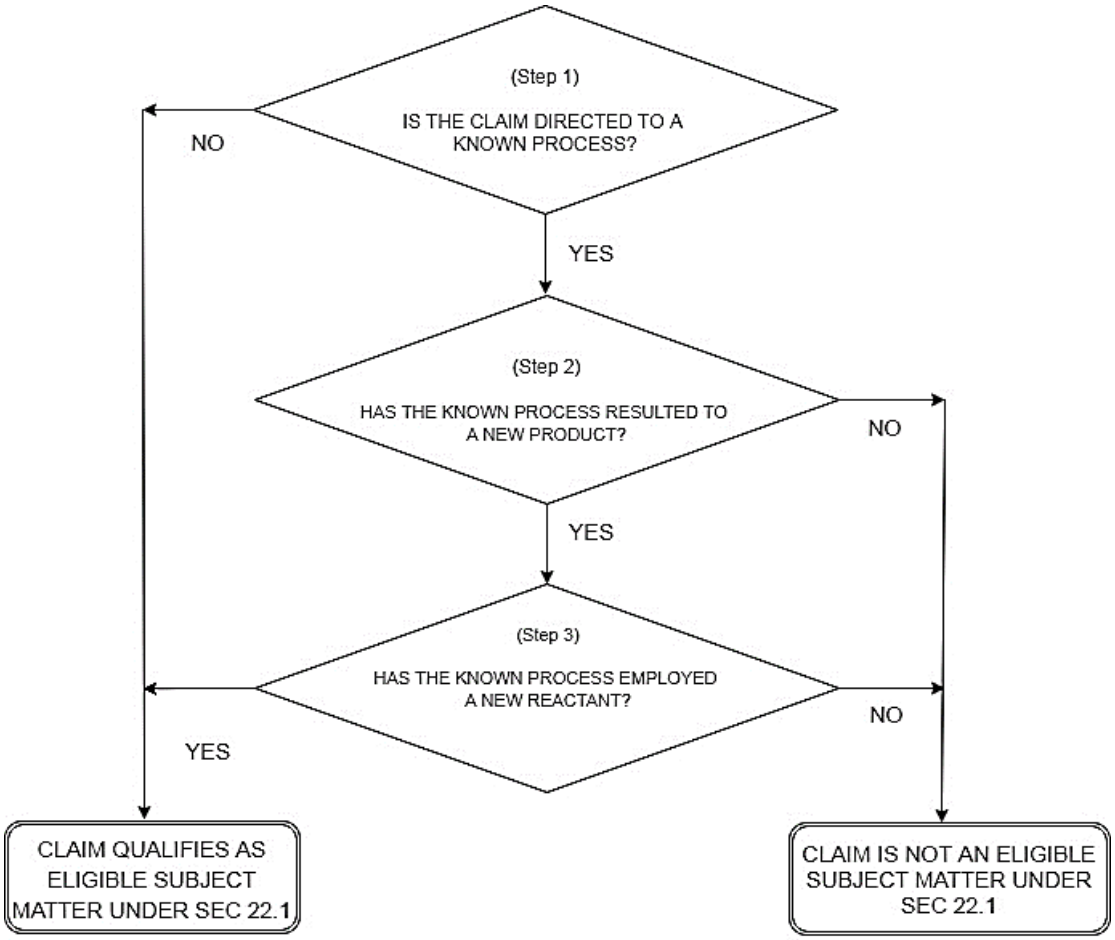

Figure 3. Flowchart for determining the patent eligibility of known processes under Section 22.1, as amended by RA 9502.

13.1. Illustrative Examples

The examiner may refer to the illustrative case below during patent eligibility assessment of claims directed to known processes.

<u>Concept 12</u> "Newly discovered results of known processes are not patentable because those results are inherent in the known processes"

Example 22

INVENTION: A process for preparing an oral formulation of Compound A directed at the formation of a water-soluble separating layer between the acid-sensitive core and the enteric coating, wherein the separating layer was formed *in situ* by a reaction between the ingredients in the core and in the enteric coating. The claimed process produces a Compound A formulation with three distinct layers, but starts with only two of the three layers.

PRIOR ART: A two-step process of preparing an oral pharmaceutical formulation including core ingredients such as Compound A and enteric coating ingredients, with no enteric coating process conditions. The enteric coating process conditions were maintained as a Trade Secret.

COMMENT

Though the inventors may not have recognized that a characteristic of prior art's process ingredients resulted in an *in situ* formation of a separating layer, the *in situ* formation is inherent when a) it was a natural result flowing from the combination of certain ingredients listed in the prior art's process, i.e. the combination of ingredients in the core and enteric coating ingredients necessarily resulted in *in situ* formation of a separating layer.

To establish inherency, a person of ordinary skill in the art is not required to recognize the inherent disclosure in the prior art. Thus, the absence of any disclosure of the prior art's process by which the known formulation was made is not significant.

14. Novelty

When a claim directed to new processes is deemed to be mere discovery, the same claim should be rejected as lacking novelty as well.

15. Inventive Step

A claim to a process which is not inherent in the prior art would be a patentable subject matter. However, this does not mean that such process will necessarily be inventive. The problem-solution approach will still apply during assessment on inventive step focusing on the claimed process vis-a-vis any prior process disclosed in the art.

-End-

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