# Beta-Lactam Antibiotic Allergy Delabeling Guideline and Toolkit

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Purpose
This guideline and toolkit was developed by the Provincial Antimicrobial Clinical Expert (PACE) group in collaboration with allergists from Fraser Health Authority, Vancouver Coastal Health and the Provincial Health Services Authority, to aid British Columbia Antimicrobial Stewardship (AmS) Programs, prescribers, pharmacists and nurses assess and manage patients who report a beta-lactam antibiotic (penicillin, cephalosporin or carbapenem) allergy. Recommendations are based on the review conducted by the Interior Health AmS Program, recommendations for management of penicillin allergy by members of the American Academy of Allergy, Asthma, and Immunology (AAAAI), the Infectious Diseases Society of America (IDSA), and the Society for Healthcare Epidemiology of America (SHEA), and supplemented by additional publications and local data. The Appendices and supplements list tools such as order sets and educational materials to aid the implementation of an allergy delabeling strategy that is adaptable to the needs to the individual health authorities.

Recommendations:
1. Recommendation: Conduct a comprehensive allergy interview to stratify patients into low-, medium- and high-risk categories. See TOOLKIT A – Sample Antibiotic Allergy History.
2. Recommendation: Delabel patients based on risk stratification categories.

<table>
<thead>
<tr>
<th>Allergy History</th>
<th>Risk Stratification</th>
<th>Delabeling Strategy</th>
</tr>
</thead>
</table>
| Intolerance (e.g. gastrointestinal symptoms, headache) | LOW | Delabel beta-lactam antibiotic allergy  
Patient education and counselling |
| Family history of beta-lactam allergy | LOW | Delabel beta-lactam antibiotic allergy  
Patient education and counselling |
| Pruritis without rash <br> Remote (>10 years) unknown reactions without IgE features <br> Definitive maculopapular or morbilliform rash | LOW | Amoxicillin direct OR graded challenge TOOLKIT B - Amoxicillin Challenge  
Note: Other beta-lactam antibiotics may be used in challenges |
### Beta-lactam Antibiotic Allergy Delabeling Guideline and Toolkit

<table>
<thead>
<tr>
<th>Allergy History</th>
<th>Risk Stratification</th>
<th>Delabeling Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urticaria (hives) or pruritic rashes Other immediate, IgE mediated reactions</td>
<td>MEDIUM</td>
<td>Penicilloyl poly-lysine (PPL) skin testing and amoxicillin challenge</td>
</tr>
<tr>
<td>EXCEPT anaphylaxis &amp; children</td>
<td></td>
<td>TOOLKIT A and TOOLKIT B</td>
</tr>
<tr>
<td>Note: For cephalosporin or carbapenem skin testing – consult an allergist or</td>
<td></td>
<td>immunologist</td>
</tr>
<tr>
<td>Anaphylaxis <strong>[Link to Table 2]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive skin test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent allergic reactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergy to multiple beta-lactam antibiotics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemodynamically unstable patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children with any immediate, IgE-mediated reaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed, severe systemic reactions <strong>[Link to Table 1]</strong></td>
<td>HIGH</td>
<td>Do not attempt drug provocation testing</td>
</tr>
<tr>
<td>Delayed, severe, cutaneous adverse reactions (SCARS)<strong>[Link to Table 1]</strong></td>
<td></td>
<td>Refer to an allergist</td>
</tr>
</tbody>
</table>

3. **Recommendation:** Children with immediate, IgE-mediated reactions (medium-high risk) and other high-risk histories should be referred to an allergist.

4. **Recommendation:** Obtain patient consent prior to drug provocation testing, such as direct or graded challenge or skin testing.

5. **Recommendation:** A challenge result interpretation plan should be in place that includes physical assessment, monitoring, interpretation and management **[Link to Table 4].**

6. **Recommendation:** Personnel and Setting

   6.1 **Delabeling procedures, such as direct and graded oral challenges, and penicillin skin testing can be performed in hospital or ambulatory care as long as the appropriate monitoring and resuscitation requirements are met.**

   6.2 **Some delabeling procedures, such as direct or graded oral challenges and penicillin skin testing can be performed in patients with low-risk or medium-risk histories, by trained and certified non-allergist physicians and/or clinical pharmacists.**
6.3 Allergists should perform delabeling procedures in patients with high-risk histories, such those who report anaphylaxis or if cephalosporin or carbapenem skin testing is indicated.

7. **Recommendation: Delabeling and Communication**

7.1 The results of the allergy interview, direct or graded challenge and/or skin testing should be documented in the patient’s “paper” and/or electronic health record.

7.2 If the patient is not beta-lactam antibiotic allergic, delabel the patients “paper” and/or electronic allergy record and Pharmacare profile [Supplementary Materials]

7.3 Counsel the patient on the findings and provide a pocket card [Toolkit E].

7.4 Communicate findings with the patient’s family physician, as applicable.

8. **Recommendation: Patients who report beta-lactam allergies should be evaluated using delabeling strategies, such as a comprehensive allergy history, graded challenge or skin testing. However, in patients or institutions where delabeling procedures cannot be implemented, use of beta-lactam antibiotic cross-reaction charts can be used to safely choose an alternative beta-lactam antibiotic in selected patients. [Algorithm 2]**
Background

Epidemiology

**Global and Local Prevalence.** Beta-lactam allergy is commonly reported and is a significant concern to prescribers and patients.\(^1\) Approximately 10% of the general population report a penicillin allergy, and 2% state they are allergic to cephalosporins.\(^2,3\) In BC, based on a review of 1000 patient records at Island Health, 15% and 2.2% of patients reported a penicillin and cephalosporin allergy, respectively. At BC Women’s Hospital, nearly 10% of expecting mothers who would benefit from penicillin at the time of delivery are listed as allergic.

**Over-labeling.** Despite having an allergy label, most individuals can tolerate a beta-lactam antibiotic. Approximately 90% of patients who report a penicillin allergy exhibit a negative skin test and could likely receive a penicillin.\(^4,5,6\) In many cases, presumed “allergies” are not secondary to immunological reactions but other adverse effects, such as gastrointestinal upset or other intolerances. Another reason for over-labeling of penicillin allergy may be a loss of immune reactivity over time.\(^7,8\) Patients with confirmed immediate, IgE-mediated (type I) penicillin hypersensitivity reactions lose immune reactivity over time: approximately 80% are still positive at 1 year, 60% at 1-10 years, and only 20% after 10 years. The reason for loss of immune reactivity is unknown. As such, the timing of the reaction, even if historically confirmed by a positive skin test, is of importance in assessment of beta-lactam antibiotic allergies and subsequent risk stratification.

**Clinical Consequences**

Patients who report a penicillin allergy are often prescribed non-beta-lactam antibiotics that are less effective, cause more adverse effects and may be more costly than first-line beta-lactam antibiotics.\(^1,3,6,7,8\)
Lower Efficacy. Use of alternative antibiotics (e.g., vancomycin, clindamycin, fluoroquinolones) that are often prescribed to patients with a reported beta-lactam allergy are less effective than first-line therapies. For example, patients prescribed beta-lactam antibiotics for treatment of *Staphylococcus aureus* bacteremia have a 35% lower risk of death, clear blood cultures more rapidly, and experience a lower 90-day recurrence than those prescribed vancomycin.9,10 Patients admitted to the emergency department with pneumonia, a urinary tract infection, sepsis or bacteremia have a 50 minute delay to the first dose of antibiotics if they report a penicillin allergy compared to those not reporting an allergy, and are 18% less likely to have their antibiotic regimen de-escalated.11 Patients with Gram-negative bacteremia prescribed a non-beta-lactam antibiotic have higher clinical failure than those prescribed a beta-lactam antibiotic.12

*Surgical Site Infections.* Use of alternative antibiotics in patients who report a beta-lactam allergy increases the risk of surgical site infections (SSIs) and adverse events. In head and neck surgery, use of clindamycin antibiotic prophylaxis leads to a 4-7-fold risk increase of SSIs compared to beta-lactam antibiotic prophylaxis, likely due to lack of Gram-negative bacterial coverage and/or drug resistance.13 In patients undergoing knee arthroplasty, clindamycin prophylaxis results in a 50% higher risk of revision due to infection than cloxacillin prophylaxis.14 In colon surgery, coronary bypass grafting, arthroplasty and hysterectomy, alternative antibiotic prophylaxis, with vancomycin, clindamycin gentamicin or a fluoroquinolone, results in a 50% increase in SSIs.15

*Adverse Effects.* Patients who report beta-lactam allergies have higher rates of adverse effects. Patient-reported penicillin allergy is associated with a 23% increase in *Clostridioides difficile* infection, a 13% increase in methicillin-resistant *Staphylococcus aureus* infection, a 30% increase in vancomycin-resistant *Enterococcus* infections and a 30% increase in length of hospital stay due to complications.16 Gentamicin antibiotic prophylaxis results in a 1.66 times increased risk of acute kidney injury compared to beta-lactam antibiotic prophylaxis.17
Vancomycin prophylaxis in joint arthroplasty and cardiac bypass procedures increases the risk of methicillin-susceptible *S. aureus* and Gram-negative SSIs.  

**Costs.** Treatment of patients who report a penicillin allergy is more costly. Such patients incur 63% higher antibiotic costs than matched controls. Use of alternative antimicrobials (e.g. vancomycin, fluoroquinolones) are up to $326.50 higher per patient than beta-lactam antibiotic therapy. In hospitalized patients who report a penicillin allergy, direct drug costs are to $609 higher per patient and indirect medical costs associated with subsequent readmissions, increased length of hospital stay and need for higher level of care (e.g. ICU), are up to $4,254 higher per patient than beta-lactam antibiotic therapy.

**Local Impact.** BC Health Authorities have also observed poorer outcomes in patients who report beta-lactam antibiotic allergies. Island Health found that sites without regular review and feedback by AmS pharmacists were nearly twice as likely to prescribe inappropriate non-beta-lactam antibiotic therapy to patients reporting a beta-lactam allergy (RR 1.85, p<0.01). Interior Health found that in patients administered alternative antibiotic surgical prophylaxis using clindamycin, ciprofloxacin or vancomycin, more than 90% could have received cefazolin, either because they did not report a beta-lactam antibiotic allergy or because of lack of cross-reactivity with the reported beta-lactam allergy. Only 7.2% of those who reported a beta-lactam allergy were candidates for alternative therapy.

**Delabeling Defined**

Allergy delabeling involves removal of the presumed allergy listing from a patient’s health record after an allergy interview and/or a negative provocation test, such as skin testing and/or direct or graded drug challenge. Removal of the allergy label from the patient’s health record can be difficult as it may be recorded in several databases. For example in BC, an allergy label may be present on the patient’s Pharmacare profile, primary physician and hospital electronic medical record and in “paper” charts. For beta-lactam allergy delabeling to be successful, the label needs to be removed from all health records, the patient needs to be informed and
understand that they are not allergic to the antibiotic as previously told, and prescribers and other health professionals need to be confident in the negative results. Otherwise, beta-lactam antibiotic allergy “re-labeling” can occur with subsequent reappearance, or ongoing persistence of the allergy label following successful delabeling. A study of long-term delabeling outcomes showed that the allergy label persisted in 51.4% electronic medical records, largely due to patients having multiple records and lack of ability of clinicians to modify them. Another study demonstrated that compliance with recommendations from de-labeling visits occurred in 75.3%; the main reason for continued avoidance of the drug was patient and health-care provider reluctance. Finally, a study of delabeled outpatients showed that 41% continued to avoid penicillin in the absence of appropriate counselling. In order to prevent re-labeling and improve adherence with recommendations after delabeling, tools such as a patient letter and pocket cards can be easily implemented. Patient counselling after each delabeling session should be thorough and pre-emptively address safety concerns.

Another strategy, administration of a non-cross-reacting beta-lactam antibiotic, such as cefazolin to a penicillin allergic patient, is not technically delabeling but can allow safe use of a beta-lactam antibiotic when provocative testing is not available or feasible. This toolkit will describe how to safely choose alternative non-cross-reacting beta-lactam antibiotics to manage beta-lactam allergy alongside delabeling, even if the allergy itself is not further investigated or deleted.

Local Barriers and Facilitators

Facilitators. All BC health authorities already have certain allergy delabeling strategies in place, the most common being allergy interviews or histories performed by nurses, pharmacists and AmS program team members, usually on patient admission. In 2018, PACE recommended that cefazolin can be used safely to provide peri-operative antibiotic prophylaxis in patients with a history of allergy to penicillins and other cephalosporins except in those who exhibited severe, delayed, cutaneous or systemic reactions. Subsequently, many BC Health Authority AmS
programs have implemented policies, guidelines and toolkits to facilitate routine administration of cefazolin for surgical prophylaxis in patients who report a beta-lactam allergy, laying the groundwork for further delabeling initiatives. Vancouver General Hospital and BC Women’s Hospital have instituted penicillin delabeling clinics for high risk patients such as those undergoing bone marrow transplant or in pregnant women in need of beta-lactam antibiotic therapy.

**Barriers.** PACE identified lack of dedicated and trained staff as the most common barrier to implementation beta-lactam antibiotic allergy delabeling strategies such as direct and graded oral challenge and skin testing. Other barriers include lack of access to allergists to perform direct oral challenge and skin testing. Tools for evaluation and management of beta-lactam antibiotic allergies, such as a standardized interview form, order sets and algorithms are also needed. Despite reported challenges, PACE explored strategies for overcoming common barriers, many of which are listed in this guideline. For example, developing a web or paper-based algorithm, would facilitate selection of safe cephalosporins in cases of penicillin allergy. To overcome lack of access to allergists, training and authorizing non-allergist physicians to perform skin testing should be explored on a provincial and health-authority level. Empowering non-allergist clinicians to perform direct oral challenge in low risk patients is another important strategy to consider.

**Goal of Delabeling**

The 2016 American Academy of Allergy, Asthma and Immunology (AAAAI) position statement encourages routine skin testing all patients who report allergies to penicillins in order to allow future use of beta-lactam antibiotics, potentially improving outcomes, decreasing costs and preventing antibiotic resistance associated with use of alternative antibiotics. However, the 2018 “Evaluation and Management of Penicillin Allergy” review, sponsored by the AAAAI, IDSA and SHEA, acknowledges the majority of patients reporting a penicillin allergy are likely to be evaluated by non-specialists because these allergies are so commonly reported and there are not enough allergists to evaluate every patient. Furthermore, with AmS programs aiming to
optimize antimicrobial prescribing, which may or may not involve a penicillin, the goal of delabeling may be secondary. In 2018, the most commonly prescribed antimicrobial in Canadian hospitals was cefazolin, followed by ceftriaxone. Except for treatment of dental infections, *Enterococcus spp.* infections and syphilis, penicillin is rarely the drug of choice. Nevertheless, penicillin allergy delabeling would facilitate use of amoxicillin, amoxicillin-clavulanate, ampicillin, cloxacillin and piperacillin-tazobactam – agents used in a wide range of common and serious infections. In an Ontario AmS beta-lactam allergy skin testing study, patients with negative test results were able to receive the preferred antibiotic, either a cephalosporin (41% of days of therapy) or a penicillin (32% of days of therapy). Therefore, beta-lactam allergy delabeling facilitates use of both penicillin’s and cephalosporins and allows for removal of the allergy label from health records for future consideration.

**AmS Delabeling Services**

AmS programs can readily adopt many components of a beta-lactam allergy delabeling service. With proper training and oversight, AmS programs can perform comprehensive allergy histories, provide patient counselling, perform direct oral or graded challenges, and delabel allergies from health records. With further training, optimally by an allergist, AmS programs can even perform skin testing and interpret results. In Ontario, AmS pharmacists and physicians have undergone specialized training and certification that included completion of certification in standard first aid and cardiopulmonary resuscitation, and injection training course (for pharmacists), a half-day observation in safety clinic, and a half-day hands-on training session by allergists on how to interpret the test. If local allergist support is available, AmS programs can help coordinate formal consultation and specialized testing. Even partial adoption of these strategies could allow delabeling of substantial numbers of patients.

**Beta-Lactam Antibiotic Allergy Delabeling – Toolkit**

[Algorithm 1-Beta-lactam antibiotic allergy delabeling process]

1.0 Allergy Interviews/Histories

*Recommendation: Conduct a comprehensive allergy interview to stratify patients into low-, medium- and high-risk categories. See TOOLKIT A – Sample Antibiotic Allergy History.*
Effect of Interviews. Allergy interviews are the first step in beta-lactam allergy investigation and are useful to identify hypersensitivity reactions as opposed to intolerances or side effects, the type and timeline of the reaction (immediate vs. delayed) and when it occurred. Allergy interviews are a very effective method to delabel patients reporting a beta-lactam antibiotic allergy. In a report of a pharmacist-led delabeling service, 80% of patients who reported a penicillin allergy could be delabeled with an interview alone as many patients equated nausea, vomiting, gastrointestinal upset, headache or dizziness with signs or symptoms of a penicillin allergy. Similarly, in a report of pharmacist-led allergy delabeling ward rounds, 25% patients who reported a penicillin allergy had non-allergic reactions, such as gastrointestinal upset, diarrhea or abdominal pain, and could be delabeled after the pharmacist confirmed the reaction in an interview. Finally, a 2019 Northern Health pharmacy residency project showed that of 49 inpatients with penicillin allergy labels, 19 were delabeled by the pharmacy resident through an allergy history lasting a mean time of 2 minutes.

Interview Components. In BC Health Authorities, the patient’s allergy status (to medications or foods) is usually documented on admission by a nurse in the “paper” and/or electronic health record. For allergy delabeling, a thorough allergy history required. There are currently no validated questionnaires or risk stratification methods for allergy interview or history. The AAAAI/IDSA/SHEA review contains a sample allergy history record that allows the interviewer to classify the reaction into intolerances, low-risk, medium-risk and high-risk histories as well as recording the timing / onset of the reaction and the when the reaction occurred (see Toolkit A). Drug hypersensitivity reactions are commonly classified by the Gell & Coombs system. Table 1 shows the Gell & Coombs drug allergy classification and associated AAAAI/IDSA/SHEA risk stratification.

The first step of the interview is to identify contraindications to the use of beta-lactam antibiotics as a class, and thus contraindications to skin testing and drug challenges. Skin testing and drug challenges should not be used in patients who report cytotoxic reactions (type II),
delayed, immune-mediated reactions (type III), and delayed severe, cutaneous adverse reactions (SCARS) (type IVb, type IVc – Stevens Johnson Syndrome, toxic epidermal necrolysis, type IVd- acute generalized exanthematous pustulosis). 26 Use of beta-lactam antibiotic allergy delabeling strategies, such as skin testing and direct or graded challenge, have not been well studied in these rare reactions and are not recommended. Such a history can often be elucidated by asking if the patient has ever been hospitalized due to the allergy or through search of medical records. Cytotoxic reactions (type II) may be drug specific. In this circumstance, a hematological consult is suggested if another beta-lactam antibiotic is required to treat the patient.

Table 1. AAAAI/IDSA/SHEA Classification of Beta-Lactam Antibiotic Allergic Reactions (Also see Algorithm 1)

<table>
<thead>
<tr>
<th>Gell &amp; Coombs Class</th>
<th>Onset</th>
<th>Clinical presentation</th>
<th>AAAAI/IDSA/SHEA Risk Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgE mediated Type I</td>
<td>Immediate 1-6 h</td>
<td>Urticaria (hives): -Onset min - hrs -Raised -Pruritic -Lesion last &lt;24 h -Fades w/out scarring Angioedema, bronchospasm, anaphylaxis</td>
<td>Low: Pruritis without rash Medium: Urticaria or other pruritic rashes; Reactions with features of IgE but not anaphylaxis High: Anaphylactic symptoms; Positive skin testing; Recurrent reactions; Reactions to multiple β-lactam antibiotics; All hemodynamically unstable patients; All pregnant patients with an IgE history</td>
</tr>
<tr>
<td>Cytotoxic Type II</td>
<td>Delayed 5-15 days</td>
<td>Hemolytic anemia, thrombocytopenia, agranulocytosis</td>
<td>High: Use of beta-lactam antibiotics not recommended unless carefully monitored. Delabeling strategies not recommended; May be drug specific without evidence of cross-reactivity. Hematology consult recommended for management and guidance of future challenges</td>
</tr>
<tr>
<td>Immune-complex mediated Type III</td>
<td>Delayed 7-21 days</td>
<td>Serum sickness, small cell vasculitis, interstitial nephritis</td>
<td>High: Use of beta-lactam antibiotics contraindicated; Delabeling strategies not recommended; Cross reactivity assessment not available</td>
</tr>
<tr>
<td>DRESS Type IVb</td>
<td>Delayed 2-6 weeks for full DRESS</td>
<td>Fever and morbilliform rash, lymph node enlargement and organ involvement e.g. bone marrow, liver, kidney, lungs</td>
<td>High: Use of beta-lactam antibiotics contraindicated; Delabeling strategies not recommended; Cross reactivity assessment not available</td>
</tr>
</tbody>
</table>
| Maculopapular rash Type IVc | Delayed 3-21 days | Maculopapular rash: - Symmetrical macules and papules that become confluent -Typically minimal or no pruritis | Low: Only if able to definitively rule out IgE mediated urticaria (hives) from a benign rash history Medium: Considering most patients as medium risk is recommended as differentiation from urticaria is difficult
The second step of the interview is to ascertain features of immediate hypersensitivity, their severity and timing. Immediate, IgE-mediated reactions, such as urticaria (hives), angioedema, wheezing and hypotension should be recorded, particularly if skin testing is being considered. Since IgE antibodies to beta-lactams antibiotics wane over time, determining if the reaction occurred over 10 years ago is also important in the risk assessment. Anaphylaxis, which increases the risk of drug provocation tests and warrants allergist assessment, should be ruled out. Anaphylaxis is defined in Table 2.

Table 2. Definition of Anaphylaxis

Anaphylaxis is likely when any ONE of the following criteria is fulfilled:

1) Acute onset of an illness involving skin, mucosal tissue, or both (generalized hives, pruritis or flushing, swollen lips-tongue-uvula) AND AT LEAST ONE OF THE FOLLOWING:
   a. Respiratory compromise (dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
   b. Reduced BP or associated symptoms (hypotonia, collapse, syncope, incontinence)

2) TWO OR MORE OF THE FOLLOWING that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours)
   a. Involvement of the skin mucosal tissue (e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)
   b. Respiratory compromise (dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
   c. Reduced BP or associated symptoms (hypotonia, collapse, syncope, incontinence)
   d. Persistent gastrointestinal symptoms (crampy abdominal pain, vomiting)
Reduced BP after exposure to a KNOWN allergen for that patient (minutes to several hours)

a. Systolic BP <90mmHg or >30% decrease from baseline

The third step is to investigate patients who report a history of “rash” to differentiate delayed, low risk, maculopapular or morbilliform rash from immediate, IgE- mediated rashes, such as urticaria (hives). Since these immediate, IgE-mediated reactions usually occur within 1-4 hours after initial drug administration, timing is of key importance, especially since both types of rashes can look similar and be associated with pruritus.

Finally, the fourth step of an allergy interview is to rule out reactions that are intolerances, reports of inefficacy or those entered in error. Many patients, upon questioning, deny they ever experienced an allergy, have been previously delabeled, or may have mistakenly reported an allergy to express a family history or treatment preference.

Interviewers. Comparative data identifying the optimal health care provider to conduct allergy interviews is lacking. While allergists are in the ideal position to take comprehensive drug allergy histories, published reports support the roles of pharmacists, non-specialist physicians, infectious disease specialists, nurses and students. The efficacy of a provider group in collecting a thorough history is dependent on the quality of the questionnaire, the perceived level of importance of allergy labels and the clinical context. For example, an Island Health 2017/2018 residency project demonstrated that after education sessions to nurses, allergy documentation on general medicine wards did not improve compared to the pre-intervention period. However, this was likely due to the fact that a single question: “Do you have any allergies?” was asked as part of a mandatory allergy screen at admission as opposed to a using a structured, thorough questionnaire. Inversely, three research projects in two BC health authorities showed that pharmacists and pharmacy students were effective in collecting allergy histories and their documentation. Furthermore, recent studies describe successful delabeling initiatives, including structured interviews, by all members of AmS teams. As such, evidence
supports encouraging any willing clinician to ascertain the necessary information to investigate
the allergy, providing they receive adequate training and use a good quality interview guide.

2.0 Risk Stratification

Recommendation: Delabel patients based on risk stratification categories

Table 3. Delabeling strategy based on allergy history

<table>
<thead>
<tr>
<th>Allergy History</th>
<th>Risk Stratification</th>
<th>Delabeling Strategy</th>
</tr>
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<tbody>
<tr>
<td>Intolerance (e.g. gastrointestinal symptoms, headache)</td>
<td>LOW</td>
<td>Delabel beta-lactam antibiotic allergy Patient education and counselling</td>
</tr>
<tr>
<td>Family history of beta-lactam allergy</td>
<td>LOW</td>
<td>Delabel beta-lactam antibiotic allergy Patient education and counselling</td>
</tr>
<tr>
<td>Pruritis without rash Remote (&gt;10 years) unknown reactions without IgE features Definitive maculopapular or morbiliform rash</td>
<td>LOW</td>
<td>Amoxicillin direct OR graded challenge TOOLKIT B – Amoxicillin Challenge Note: Other beta-lactam antibiotics may be used in challenges</td>
</tr>
<tr>
<td>Urticaria (hives) or pruritic rashes Other immediate, IgE mediated reactions EXCEPT anaphylaxis &amp; children</td>
<td>MEDIUM</td>
<td>Penicilloyl poly-lysine (PPL) skin testing and amoxicillin challenge TOOLKIT A and TOOLKIT B Note: For cephalosporin or carbapenem skin testing – consult an allergist or immunologist</td>
</tr>
<tr>
<td>Anaphylaxis [Link to Table 2] Positive skin test Recurrent allergic reactions Allergy to multiple beta-lactam antibiotics Hemodynamically unstable patients Children with any immediate, IgE-mediated reaction Delayed, severe systemic reactions [Link to Table 1]</td>
<td>HIGH</td>
<td>Do not attempt drug provocation testing Refer to an allergist</td>
</tr>
</tbody>
</table>
**Delayed, severe, cutaneous adverse reactions (SCARS)** [Link to Table 1]

**Low Risk.** Patients who report intolerances (e.g., nausea and vomiting) or have low-risk histories (e.g., family history of penicillin allergy) can usually receive the offending beta-lactam antibiotic after education that the history does not constitute an allergy. Their record can be updated to reflect this. Those with a history of pruritis without rash or remote/unknown reactions without clear Ig-E features should be offered a direct or graded amoxicillin challenge under observation to comprehensively delabel the allergy. While the AAAAI/IDSA/SHEA review questions the interviewer’s ability to make a distinction between immediate, IgE-mediated urticarial rashes (hives) and delayed maculopapular/morbilliform rashes, reactions clearly identifiable as such can be managed as low risk.

**Medium Risk.** Patients with medium-risk histories, who report urticaria (hives), or other immediate, IgE-mediated reactions other than anaphylaxis, can be managed with a skin test and direct or graded challenge. Those who report a penicillin allergy should receive a penicillin skin test followed by an oral amoxicillin challenge, if the skin test is negative. Patients who report a “rash” where the possibility of an immediate, IgE-mediated reaction (such as urticaria) cannot be definitely ruled-out should be considered medium risk and ideally offered skin testing. Of note, most patients who report a delayed-onset rash (i.e. more than 4 hours after antibiotic receipt) can be successfully classified as low risk since this is most consistent with a delayed type IV reaction.

**High Risk.** Patients with high-risk histories including anaphylaxis, positive penicillin skin tests, recurrent allergic reactions to multiple beta-lactam antibiotics or hemodynamic instability should be evaluated by an allergy specialist or immunologist or undergo desensitization if a beta-lactam antibiotic treatment is required. Patients with delayed cytotoxic reactions (type II), immune-complex reactions (type III) and severe cutaneous adverse reactions (SCARs) are high risk. Such patients have not been adequately studied and should be excluded from any drug provocation tests or delabeling algorithms. Beta-lactam-induced-neutropenia is reported in approximately 10% of patients receiving long-term therapy (greater than 2 weeks).
particularly with penicillin G, the antistaphylococal penicillins (e.g. cloxacillin), piperacillin-tazobactam, ceftriaxone, cefepime and ceftaroline. The cause of these reactions is not well understood, but is theorized to be the result of an immunologic reaction that involves hypersensitivity, antibody-mediated destruction (e.g. cytotoxic – Type II – reaction), or a combination of both. Without discontinuation of the offending beta-lactam antibiotic, the reaction can progress to agranulocytosis (with an absolute neutrophil count less than 0.1 x 10^9/L). Neutropenia can be accompanied by eosinophilia and/or thrombocytopenia. Symptomatic symptoms, such as fever and rash may be present in approximately 25% of cases. If continued beta-lactam antibiotic therapy is required after discontinuation of the offending drugs, an alternative antibiotic with low or absent risk of cross-reactivity can be used, such as one with a different R₁ side chain or different class, when the clinical benefits of beta-lactam antibiotic therapy outweigh the low but potential risk of sustained neutropenia.

2.0 Pregnant Patients

Recommendation: Pregnant patients who report a beta-lactam allergy should be classified into low-, medium- and high-risk categories and offered delabeling strategies.

The AAAAI/SHEA/IDSA review refers to pregnant patients as high risk and cites that “skin testing is infrequently performed in pregnancy”. However, published data and local clinical experience support delabeling strategies in pregnant women. As such, it is generally felt that the AAAAI/SHEA/IDSA review recommendations are overly cautious in recommending allergist referral for all pregnant patients.

Pregnancy does not affect the likelihood of reactivity or cross-reactivity in a patient with a history of an allergy, allowing classification of the reaction recorded in an allergy history into low-, medium- and high-risk categories. Pregnant patients reporting side-effects and intolerances can be educated and offered the offending drug. Those who report features of immediate, IgE-mediated allergic reactions, such as hives or angioedema, should be referred for
skin testing, as any medium-risk patient. Those with high-risk histories described above should be referred for allergist assessment and not treated or tested with beta-lactam antibiotics.

A notable gap in the literature pertains to management of delayed type IV reactions, namely low risk macropapular rashes, using direct or graded oral challenge. Studies describing delabeling pregnant patients, regardless of the immunological basis for the rash, all perform skin testing first to rule out a type I reaction. The authors and contributors of this toolkit agree that pregnant women with histories lacking IgE features can likely be offered the implicated drug (e.g. given penicillin for Group B Strep prophylaxis) or delabeled using an observed oral challenge, similarly to the published approach in non-pregnant patients. However, studies in pregnant women are lacking. Current efforts are underway to describe the use of direct oral challenge without skin testing in low-risk pregnant patients reporting mild rashes to beta-lactam antibiotics.

### 3.0 Pediatric Patients

*Recommendation: Children with immediate, IgE-mediated reactions (medium-high risk) and other high-risk histories should be referred to an allergist.*

Children are often excluded from allergy delabeling studies and publications such as the AAAAI/SHEA/IDSA review. However, the Canadian Pediatric Society (CPS) position statement directly addresses penicillin allergy in pediatric patients and young adults.32

Beta-lactam antibiotic allergy prevalence in children at 5-8% is lower than in adults at 10%. Nevertheless, 94-96% of children tolerate a beta-lactam antibiotic challenge upon further evaluation, due to misdiagnosis of an allergy or waning antibodies. Like adults, many children can be delabeled using a thorough allergy assessment questionnaire with the caregiver [Toolkit A](#). Of note, unlike adults, maculopapular rash in children is more commonly associated with infection rather than allergy.
Like adults, children can be risk stratified in low-, medium- and high-risk categories based on the allergy interview. Like adults, many children can be delabeled through an allergy interview with a parent or caregiver. Children who report low-risk histories, can receive the medication again or undergo an observed oral challenge (e.g., amoxicillin 15 mg/kg PO). Children who have immediate, IgE-mediated reactions or delayed, severe systemic or cutaneous reactions should be referred to an allergist. While adults with immediate, IgE-mediated reaction histories can be delabeled through skin testing, this strategy is less useful in children, as the test has lower positive and negative predictive value. Therefore, the CPS statement de-emphasizes skin testing in children, and reserves it only in special circumstances as part of an assessment by an allergist.

**Drug Provocation Tests**

*Description.* Beta-lactam allergy delabeling strategies, using drug provocation tests such as oral challenge and skin/intradermal tests, are the gold standard for identification of drug hypersensitivity reactions.

**4.0 Patient Consent**

**Recommendation:** Obtain patient consent prior to drug provocation testing, such as direct or graded challenge or skin testing.

*Consent.* Prior to undertaking any drug provocation testing, consent should be obtained from the patient, and documented in the health record according to local policy. The patient should be informed that up to 10% of patients can experience a reaction such as a rash, pruritis or anxiety, but these reactions are often mild and treatable. The patient should be counselled on any self-monitoring parameters after the direct observation period ends.

**Graded and Direct Challenge**

*Description.* In a graded challenge, fractional doses of the antibiotic, usually one-tenth to one-fourth of the full dose are administered, followed by a 30- to 60-minute monitoring period.
tolerance is observed, administration of a full dose of the desired drug follows, with a final 30-
to 60-minute period of monitoring. Three-step challenges (giving 1/100th, 1/10th and finally the
full dose) have also been described, but the additional step is seen as redundant. The initial
dose exposes the patient to a small amount of drug, followed by a period of close observation
in case of a reaction, which in cases of non-specific symptoms such as rash or nausea, would
theoretically be milder and more manageable than with a full dose. For penicillin allergic
patients, a graded challenge is conducted with oral amoxicillin, which has the both the
immunologically significant core beta-lactam ring and R-group side chain. Penicillin is not
recommended for demonstrating penicillin tolerance because selective allergy to ampicillin and
amoxicillin has been described. Graded challenges have also been successfully reported with
oral and intravenous cephalosporins.

Graded challenges are safe but need to be conducted in a controlled and protocolized fashion,
with an allergic reaction treatment plan in place. In a study of patients with low- and medium-
risk histories, use of a 2-step amoxicillin graded challenge with a 30-minute observation period
resulted in no reaction in the majority (77.4%) and nonallergic reactions in most of the
remainder (20%). Only 2.6% experienced allergic reactions, with 1 patient (0.7%) requiring
treatment with an antihistamine. In a similar study of low-risk patients with a remote (>10 year)
history of penicillin cutaneous-only allergy, administration of a monitored two-step graded
amoxicillin challenge, using one-tenth the target dose then administration of the full dose
resulted in no reaction in the majority (96.2%) of patients. The remaining (3.8%) of patients
experienced mild cutaneous reactions managed with an antihistimine.

Direct full-dose challenges should also be administered in a controlled and protocolized fashion
under observation much like graded challenges. Toolkit B contains sample direct oral
amoxicillin challenge orders.

The AAAAI/IDSA/SHEA review suggests that a direct full-dose challenge can be performed in
patients with low-risk histories under medical supervision. Graded challenges are more
inconvenient as they require a longer observation period and are more costly as the smaller
dose requires either a liquid formulation or specialty compounding. Considering these implications, direct challenges are preferred, with graded challenges reserved for special circumstances (e.g., prescriber or patient preference). A comparison of full-dose direct and 2-step graded challenges in patients with low-risk allergy histories to a variety of medications found the reaction rate and severity did not significantly differ (6 vs. 12%, p=0.06) with the majority of reactions in those receiving a two-step challenge occurring after administration of the second full dose. Although the majority of patients had a history of beta-lactam antibiotic allergy, the reaction rate for beta-lactam antibiotic allergic patients was not specifically reported. This study implies that full-dose direct and graded challenges have similar safety in patients with low-risk histories.

5.0 Result Interpretation

Recommendation: A challenge result interpretation plan should be in place.

Table 4. Management of drug challenge reactions (adapted from reference 26)

<table>
<thead>
<tr>
<th>Response to Challenge</th>
<th>Actions</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjective Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritis without rash</td>
<td>Obtain vital signs</td>
<td>If no objective signs of reaction, symptoms unlikely an allergic reaction</td>
</tr>
<tr>
<td>Scratchy throat, tongue or palate</td>
<td>Perform physical exam looking for objective signs to support a minor cutaneous or systemic reaction</td>
<td></td>
</tr>
<tr>
<td>Vague gastrointestinal symptoms (e.g. nausea)</td>
<td>Increase observation time by 30 minutes to observe for objective signs</td>
<td>If objective signs of reaction, consider following “Possible systemic (anaphylactic) reaction” pathways below Consider specialty evaluation</td>
</tr>
<tr>
<td>Minor cutaneous reaction</td>
<td>Obtain vital signs</td>
<td>Patient labeled as penicillin (beta-lactam antibiotic) allergic</td>
</tr>
<tr>
<td>Flushing</td>
<td>Perform physician exam looking for rash type and extent, as well as any other signs suggestive of a systemic (anaphylactic) reaction</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>Treat with an antihistamine</td>
<td></td>
</tr>
<tr>
<td>Urticarial (hives)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Response to Challenge</strong></td>
<td><strong>Actions</strong></td>
<td><strong>Interpretation</strong></td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Increase observation time by 30 minutes to observe for signs of systemic reaction or symptom resolution</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Possible systemic (anaphylactic reaction)**

*Typically involves ≥ 2 organ systems*

- Cutaneous: pruritus, flushing, rash, urticarial (hives) or swelling
- Respiratory: nasal congestion, runny nose, cough, shortness of breath, chest tightness, wheezing
- Cardiovascular: faintness, tachycardia, tunnel vision, chest pain, hypotension, sense of impending doom, loss of consciousness
- Gastrointestinal: nausea, vomiting, cramping, diarrhea

*Hypotension alone in the setting of a known allergen exposure is also considered anaphylaxis*

**Assess, airway, breathing, circulation**

**Obtain vital signs**

**Place patient in supine position and elevate legs**

**Call a CODE BLUE and if automated external defibrillator available, retrieve and bring to bedside**

**Administer intramuscular epinephrine mid-upper thigh, and repeat every 5-15 minutes as needed**

**Administer oxygen and intravenous fluids**

**Administer adjunctive treatments such as antihistamine, steroids and bronchodilators**

**Patient labeled as penicillin (beta-lactam antibiotic) allergic**

**Consider specialty evaluation**

---

*Result Interpretation.* Most reactions are minor subjective symptoms such as pruritis without rash, scratchy throat or palate or vague gastrointestinal symptoms. Most commonly, these include perioral tingling, pruritus without urticaria, throat and lip discomfort, headache, tachycardia, and nausea. These may be anxiety-related, and spending time with the patient explaining the safety of challenge procedures in advance may help to reduce the incidence of these nonspecific reactions. If performing a graded challenge, absence of an immediate reaction after 30-60 minutes of observation allows administration of a full dose. Demonstration of amoxicillin tolerance enables future use of all beta-lactam antibiotics, including penicillin, unless reactions to multiple drugs from different classes are present.
Skin Testing

Description. Skin testing, combined with an oral amoxicillin challenge is recommended to evaluate patients with medium-risk histories who report immediate, IgE-mediated reactions to penicillin, such as urticaria or angioedema, EXCLUDING anaphylaxis. The positive predictive value of a penicillin skin test is approximately 50% for an immediate hypersensitivity reaction. The negative predictive value of the penicillin skin test is 84-99% for an immediate hypersensitivity reaction (higher if minor determinant mixture is tested in addition to penicilloyl-polylysine).

In Canada, the benzylpenicilloyl polylysine [Pre-Pen®] is commercially available for administration by puncture (prick, scratch) or intradermal injection, at a cost of approximately $50. Pre-Pen® does not include the minor allergenic determinants. These can be compounded by pharmacy using parenteral penicillin G. Compounding instructions and stability details are available in the Supplementary Materials.

Skin test reagents for the other beta-lactams antibiotics, such as cephalosporins, are described in published case-reports, and would need to be compounded from the injectable form of the drug. The predictive value these non-penicillin beta-lactam antibiotic skin reagents is unknown. Although a positive skin test result is suggestive of an IgE-mediated allergy, a negative result does not necessarily rule out sensitivity. As true cephalosporin allergy is uncommon, need for skin testing in patients with medium-risk histories would be low. Allergist assessment is recommended for cephalosporin or carbapenem skin testing.

Methods of Skin Testing. Penicillin skin testing in Canada is conducted using 4 components: (1) benzylpenicilloyl polylysine [Pre-Pen® skin test reagent] to test for the major determinant; (2) compounded penicillin G for the minor determinants; (3) histamine for positive control; and (4) saline as the negative control. The tester first performs the prick/scratch test and the intradermal injection is typically performed if the prick test is negative. Procedures that omit the initial prick or scratch test and employ solely the intradermal test have also been described. The testing is performed using a step-wise skin-based evaluation which is included with the Pre-Pen® kit, and results can be read 15 minutes after reagents are scratched into the skin or placed
intradermally. Patients with a positive skin test result are allergic to penicillin and should not be challenged. A well-validated approach, with a negative predictive value of nearly 100%, involves an oral challenge with amoxicillin for those with negative skin test results. The penicillin allergy can be subsequently removed from the patient’s profile and the patient can be considered delabeled. The details of this procedure are described in Toolkit C.

6.0 Setting and Personnel

Recommendation:

6.1 Delabeling procedures, such as direct and graded oral challenges, and penicillin skin testing can be performed in hospital or ambulatory care as long as the appropriate monitoring and resuscitation requirements are met.

6.2 Some delabeling procedures, such as direct or graded oral challenges and penicillin skin testing can be performed in patients with low-risk or medium-risk histories, by trained and certified non-allergist physicians or by clinical pharmacists.

6.3 Allergists should perform delabeling procedures in patients with high-risk histories, such as those who report anaphylaxis or if cephalosporin or carbapenem skin testing is indicated.

Setting and Personnel. Oral challenges can be performed in an inpatient or outpatient setting as long as the following criteria are met:

- involved staff receive sufficient education;
- clinical decision support/management algorithm in place;
- anaphylaxis treatment protocols in place;
- nursing observation protocols in place;
- pharmacy compounding and/or preparation protocols in place, if applicable;
- access to anti-allergy medication;
- pharmacy can compound graded challenge antibiotic (if applicable).
Inpatients should be stable from a hemodynamic and respiratory perspective. H1 antihistamines and IM epinephrine (with a pre-measured dose pre-calculated) should be readily available. Because graded challenges will not prevent or circumvent an immediate allergic reaction, the clinician must be prepared to recognize and treat such a reaction if one occurs. Graded or direct challenge can be administered by non-allergists, as long as appropriate training is undertaken.

Similarly, penicillin skin testing can be performed in an inpatient or outpatient setting as long as the following criteria are met:

- involved staff receive sufficient education;
- clinical decision support/management algorithm in place;
- access to anti-allergy medication;
- anaphylaxis treatment protocols in place;
- nursing observation protocols in place;
- pharmacy compounding and/or preparation protocols in place, if applicable;
- skin testing inclusion and exclusion criteria established;
- pharmacy can compound graded challenge antibiotic (if applicable).

Allergists are in the optimal position to perform skin testing based on their formal training and experience. Coordination of care between AmS teams and allergists has been shown to increase delabeling and subsequent use of beta-lactam antibiotics with associated cost savings. With beta-lactam antibiotic allergy labels being so prevalent, there are likely not enough allergists in BC health authorities to whom all patients with low- and moderate-risk histories can be referred for evaluation and drug provocation testing. AmS teams are increasing offering delabeling services in these patients. The beta-lactam antibiotic allergy services offered by AmS programs may vary by resource availability and training in each health authority. Table 5 lists suggested beta-lactam antibiotic allergy AmS services and requirements.

Table 5. Suggested AmS Beta-lactam Allergy Delabeling Services and Requirements

<table>
<thead>
<tr>
<th>Delabeling Service</th>
<th>Allergy History</th>
<th>Requirements</th>
<th>Comments</th>
</tr>
</thead>
</table>


**Beta-lactam Antibiotic Allergy Delabeling Guideline and Toolkit**

<table>
<thead>
<tr>
<th>Beta-lactam antibiotic allergy history + Direct or graded amoxicillin challenge + Penicillin skin testing</th>
<th>Medium-risk</th>
<th>As above + Certification to perform penicillin-skin testing (e.g. for AmS or ID physician) Pharmacy ability to compound minor determinant mixture Order forms, clinical decision support tools, monitoring and resuscitation protocols in place</th>
<th>Cephalosporin or carbapenem skin testing should be referred to an allergist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-lactam antibiotic allergy history + Direct or graded amoxicillin challenge + Penicillin skin testing</td>
<td>High-risk</td>
<td>Allergist referral</td>
<td></td>
</tr>
<tr>
<td>Beta-lactam antibiotic allergy history + Direct or graded amoxicillin challenge + Penicillin skin testing</td>
<td>Low-Risk</td>
<td>Comprehensive Allergy Interview Questionnaire <strong>Toolkit A</strong></td>
<td>Can be used to delabel substantial numbers of low-risk patients who report beta-lactam antibiotic intolerance or family history</td>
</tr>
</tbody>
</table>

Antihistamines (e.g., diphenhydramine or dimenhydrinate), and systemic corticosteroids can lead to a false negative skin test, ideally patients should avoid taking them prior to assessment. Tricyclic antidepressants, topical steroid preparations and topical tacrolimus
interfere can with skin test results. Montelukast and H2-blockers, such as ranitidine, have no effect on test interpretability.

7.0 Documentation and Communication

Recommendation: In patients who are not beta-lactam antibiotic allergic, document findings and delabel patient “paper” and/or electronic medical health records; delabel Pharmacare records [Supplementary Materials] and communicate findings with the patient or patient caregiver and family physician, as applicable.

7.1 The results of the allergy interview, direct or graded challenge and/or skin testing should be documented in the patient’s “paper” and/or electronic health record.

7.2 If the patient is not beta-lactam antibiotic allergic, delabel the patients “paper” or electronic allergy record and Pharmacare profile [Supplementary Materials]

7.3 Counsel the patient on the findings and provide a letter and pocket card [Toolkit D] [Toolkit E].

7.4 Communicate findings with the patient’s family physician, as applicable.

8.0 Cross-reactivity between Beta-lactam Antibiotics

Cross-reactivity charts to choose alternative beta-lactam antibiotics in selected patients.

Recommendation: Delabeling strategies are preferred when evaluating reported beta-lactam allergies. However, in patients or institutions where delabeling procedures cannot be implemented, use of beta-lactam antibiotic cross-reaction charts can be used to safely choose an alternative beta-lactam antibiotic in selected patients. [Algorithm 2]

In patients who report a beta-lactam allergy, delabeling as previously described is preferred. However, it is now recognized that cross-reactivity between penicillin and other beta-lactam antibiotics, such as the cephalosporins, carbapenems and aztreonam has been over-estimated, and is now believed to be related to side chain similarity rather than commonality of the beta-lactam ring. Published algorithms and charts can be used to select non-penicillin beta-lactam antibiotics in patients who report a penicillin allergy. [Algorithm 2] shows cross-reactivity of beta-lactams antibiotics based on side-chain similarity developed by Interior Health. As with direct provocative testing, use of this chart to select non-cross-reacting beta-
**Beta-lactam Antibiotic Allergy Delabeling Guideline and Toolkit**

Lactam antibiotic therapy should be avoided in patients with severe, delayed cutaneous and systemic reactions or who have exhibited hypersensitivities to multiple beta-lactam antibiotics. For health authorities or hospitals unable to fully implement a penicillin delabeling program, use of beta-lactam antibiotic cross-allergy charts and algorithms may be useful to select alternative antibiotic therapy.

After the allergy interview and risk stratification, cross-reactivity information can be used to evaluate the safety of the intended beta-lactam antibiotic regardless of the drug implicated in the reported reaction. As the basis for cross-reactivity is IgE antibodies from published beta-lactam skin testing reports, these algorithms and tables are most useful in guiding therapy selection for patients with immediate, IgE-mediated reactions (mainly patients with medium-risk histories). Algorithm 1 illustrates how use of a cross-reactivity chart can be used to select a non-cross-reacting beta-lactam antibiotic in patients reporting a beta-lactam allergy.

Patients with low-risk beta-lactam allergy histories who report non-allergic symptoms, such as gastrointestinal intolerance, a family history of penicillin allergy, pruritus without rash, or remote or unknown reactions, can likely receive any penicillin, cephalosporin, carbapenem or aztreonam under observation regardless of cross-reactivity risk.

For patients with medium-risk penicillin allergy histories who report immediate, IgE-mediated reactions such as urticaria and angioedema, cross-reactivity based on R₁ side chain similarity should be assessed using a guide such as Algorithm 3. If there is no cross-reactivity between the offending and the intended beta-lactam antibiotic required for treatment, the intended antibiotic may be given. If there is no cross-reaction with the intended beta-lactam is possible, and no other alternatives exist, the patient should undergo skin testing (if the reported allergy is to penicillin; Toolkit D), followed by a challenge of the intended beta-lactam if the results are negative; alternatively, they may be prescribed a non-beta-lactam antibiotic.

Cross-reactivity tables can also be used to select non-reacting alternatives in patients with high risk IgE-mediated histories such as anaphylaxis. For example, anaphylaxis from penicillin is not a contraindication to cefazolin, ceftriaxone, or carbapenem use.

**Other Considerations**
**Allergist Referral.** Certain patients are not candidates for delabeling by non-specialists and should be referred to an allergist.\(^{26}\) Indications for referral include:

- History of anaphylaxis;
- History of anaphylaxis and need for desensitization;
- History of recurrent reactions;
- Reactions to multiple beta-lactam antibiotics;
- Need for cephalosporin or carbapenem skin testing;
- History of positive skin testing;
- Children with a history of immediate, IgE-mediated reactions.

**Automated/System-wide Strategies.** Health authorities commonly document the patient allergy status in the “paper” and/or electronic health record. Unless a requirement, the patient’s reaction and timing are not commonly recorded, necessitating another allergy interview to obtain this information. To overcome this barrier, automated strategies, such requiring completion of the reaction description field before saving the electronic record can improve completeness and are cost-effective. A 2018 Island Health project demonstrated that a reaction description was specified 78% of the time, up from 50% at baseline, when nurses collecting the allergy history could not save the electronic history record without populating the reaction field. Pre-printed orders sets and guidelines can include recommendations on when to choose alternatives in penicillin allergy. For example, pre-operative order sets requiring cefazolin can include a statement such as “ceFAZolin can be safely administered to patients with history of allergy to penicillins including anaphylaxis EXCEPT in those with severe delayed skin reactions – e.g. Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), or drug reaction with eosinophilia and systemic symptoms (DRESS)”. Automated decision-support warning messages about potential allergy cross-reactivity spanning the entire beta-lactam group can be tailored to only pop-up when in cases where actual cross-reactivity exists (e.g. ampicillin prescribed in a penicillin allergic patient) and disabled otherwise. Allergy de-labeling guidance and cross-reactivity algorithms can be programmed into FRONTLINE\(^\text{®}\) (formerly, SPECTRUM\(^\text{®}\)), an application-based Antimicrobial Stewardship support tool.
BC PROVINCIAL ANTIMICROBIAL CLINICAL EXPERT (PACE) GROUP

BETA-LACTAM ANTIBIOTIC ALLERGY DELABELING GUIDELINE AND TOOLKIT

<table>
<thead>
<tr>
<th>Date</th>
<th>Proposal</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAY 27, 2021</td>
<td>PACE group endorses the “Beta-lactam Allergy Delabeling Guideline and Toolkit”</td>
<td>Stakeholder feedback reviewed; reformatted.</td>
</tr>
</tbody>
</table>

P&T DECISION

<table>
<thead>
<tr>
<th>Date</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEPTEMBER 23, 2021</td>
<td>BC Health Authority Pharmacy and Therapeutics Committee endorses the “Beta-lactam Allergy Delabeling Guideline and Toolkit”</td>
</tr>
</tbody>
</table>

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References:


25. American Academy of Allergy, Asthma and Immunology. Penicillin allergy testing should be performed routinely in patients with self-reported penicillin allergy. J Allergy Clin Immunol Pract 2017;


Algorithm 2. Safe Alternative Beta-lactam Antibiotic Selection in Allergic Patients

1. **Patient reports beta-lactam allergy**
   - **Perform an allergy history**

2. **If allergy history unobtainable**
   - (try to rule out high-risk history from health records or contacts)

   - **History of serious systemic reaction:**
     -Interstitial nephritis
     -Small vessel vasculitis
     -Hematological reactions (e.g., hemolytic anemia, neutropenia, thrombocytopenia)
     -Serum sickness
     -Drug fever

   - **History of delayed, severe, cutaneous adverse reaction (SCARs):**
     -Stevens-Johnson syndrome
     -Toxic epidermal necrolysis
     -Acute generalized exanthematous pustulosis
     -Drug reaction with eosinophilia and systemic symptoms (DRESS)

3. **YES**
   - **HIGH RISK**
   - Use of beta-lactam antibiotics contraindicated
   - Consult allergist, Infectious Diseases or AmS for further management

4. **NO**
   - **Intolerance (e.g., GI upset, nausea, vomiting, headache)**
   - **Family history of allergy**

   - **YES**
     - Discuss with patient
     - Low risk reaction will recur
     - Can likely receive any beta-lactam antibiotic

   - **NO**
     - Use Beta-lactam Antibiotic Cross-allergy Chart to select alternative antibiotic

   - **Delabel patient health records**

5. **Go to Algorithm 3**
Algorithm 3. Beta-lactam Antibiotic Cross-Allergy Chart

* Also applies to beta-lactamase inhibitor combinations (amoxicillin-clavulanate and piperacillin-tazobactam)
## Toolkit A

### Antibiotic Allergy History

**Reported Antibiotic Allergy**

- □ Penicillin
- □ Amoxicillin
- □ Other antibiotic (specify): ____________________________

**Date of Reaction:** ____________________________

**Reaction Details** (check all that apply)

<table>
<thead>
<tr>
<th>High risk: Contraindicated Penicillin skin testing/challenge (potential, severe, non-immediate reactions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Stevens Johnson syndrome (rash with mucosal symptoms)</td>
</tr>
<tr>
<td>□ Organ injury (e.g. liver, kidney)</td>
</tr>
<tr>
<td>□ Acute generalized exanthematous (rash with pustules)</td>
</tr>
<tr>
<td>□ Serum sickness (rash with joint pain, fever, myalgia)</td>
</tr>
<tr>
<td>□ Erythema multiforme (rash with target lesions)</td>
</tr>
<tr>
<td>□ Drug reaction with eosinophilia and systemic symptoms (DRESS) (rash with eosinophilia and organ injury)</td>
</tr>
</tbody>
</table>

*Adapted from JAMA 2018; 321: 188-199*
**Toolkit A**

**Antibiotic Allergy History**

Other symptoms:

<table>
<thead>
<tr>
<th>Timing / Onset</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate (&lt;4 hrs)</td>
<td>None/penicillin continued</td>
</tr>
<tr>
<td>Intermediate (4-24 hrs)</td>
<td>Steroid (IV or PO)</td>
</tr>
<tr>
<td>Delayed (&gt;24 hrs)</td>
<td>Penicillin discontinued</td>
</tr>
<tr>
<td>Unknown</td>
<td>Other: ________________________</td>
</tr>
</tbody>
</table>

How long ago was the reaction?
- <6 mo
- 6-mo - 1 yr
- 2-5 yrs
- 6-10 yrs
- >10 yrs
- Unknown

Other beta-lactam antibiotic use
- Previous use of a penicillin or other beta-lactam (prior to course that caused reaction)
  - If yes, please list drugs:

- Subsequent use of penicillin or other beta-lactam (after the course that caused reaction)
  - If yes please list drugs:

History taken by:
Printed name: ____________________  Signature: ____________________  Date: _____________

Adapted from JAMA 2018; 321: 188-199
Toolkit B
Amoxicillin Two-Step (Graded) Challenge

Testing is not necessary if a penicillin class antibiotic has been tolerated since the index reaction.

**NOTE:**
- Skin testing is preferred for patients with clear IgE histories (e.g. urticaria, angioedema, wheezing).
- Challenges should be performed only after careful consideration of the potential benefit to the patient in question, weighed against the risk of potential harm from an allergic reaction.

**DO NOT** perform any penicillin allergy testing if there is a history of penicillin-associated:

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blistering rash</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
</tr>
<tr>
<td>Nephritis</td>
</tr>
<tr>
<td>Hepatitis</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Joint pain</td>
</tr>
</tbody>
</table>

This testing is indicated if:
- The reaction was cutaneous
- The reaction had features of IgE / immediate hypersensitivity
- The patient currently unstable or compromised hemodynamic or respiratory status or is pregnant with low risk allergy history

This test may also be used for low-risk reactions that include:
- Remote (>10 yrs) unknown reactions without features of IgE
- Pruritis without rash
- Isolated reactions that are unlikely (e.g. gastrointestinal symptoms, headaches)

Adapted from JAMA 2018; 321: 188-199
Toolkit B
Amoxicillin Two-Step (Graded) Challenge

Ordered by: _____________________ Performed by: _____________________ Date: _____ / _____ / _____

1
Amoxicillin oral challenge given: □ 25 mg □ 50 mg

Time given: ________ Time observed: ________

Time given: □ 30 min □ 60 min Observation ended: ________

Observed challenge reaction
□ None □ Yes (list signs and symptoms)

Time onset: ____________

Observed challenge reaction treatment given
□ None □ Yes (list signs and symptoms)

2
Amoxicillin oral challenge given: □ 250 mg □ 500 mg

Time given: ________ Time observed: ________

Time given: □ 30 min □ 60 min Observation ended: ________

Observed challenge reaction
□ None □ Yes (list signs and symptoms)

Delayed challenge reaction reported
□ None □ Yes (list signs and symptoms)

Time onset: ____________

Observed challenge reaction treatment given
□ None □ Yes (list signs and symptoms)

Delayed challenge reaction treatment given
□ None □ Yes (list signs and symptoms)

Adapted from JAMA 2018; 321: 188-199
Penicilloyl-Polylysine (PPL) Skin Testing

**DO NOT perform any penicillin allergy testing if there is a history of penicillin-associated:**

<table>
<thead>
<tr>
<th>Blistering rash</th>
<th>Hemolytic anemia</th>
<th>Nephritis</th>
<th>Hepatitis</th>
<th>Fever</th>
<th>Joint pain</th>
</tr>
</thead>
</table>

This testing is indicated if:
- The reaction was cutaneous
- The reaction had features of IgE / immediate hypersensitivity
- The patient currently unstable or compromised hemodynamic or respiratory status or is pregnant with low risk allergy history

**Skin Testing:**
- Place test on arms
- Place test and read all puncture tests prior to placing any intradermal tests.
- Positive tests are interpreted as wheal ≥ 5 mm with flare greater than wheal.
- **Do not record test if saline control is positive or histamine control is negative.**

<table>
<thead>
<tr>
<th>1 Prick / Puncture Test</th>
<th>2 Intradermal Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time placed:</td>
<td>Time placed</td>
</tr>
<tr>
<td>Time read:</td>
<td>Time read:</td>
</tr>
<tr>
<td>PPL</td>
<td>wheal flare</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>PPL</td>
</tr>
<tr>
<td>Saline control</td>
<td>Penicillin G</td>
</tr>
<tr>
<td>Histidine control</td>
<td>Saline control</td>
</tr>
<tr>
<td></td>
<td>Histidine control</td>
</tr>
</tbody>
</table>

Adapted from JAMA 2018; 321: 188-199

**3 Amoxicillin challenge**
Penicilloyl-Polylysine (PPL) Skin Testing

<table>
<thead>
<tr>
<th>Ordered by: _____________________</th>
<th>Performed by: _____________________</th>
<th>Date: <strong>/_/</strong></th>
</tr>
</thead>
</table>

**Amoxicillin oral challenge given:**
- 250 mg
- 500 mg

**Time given:** ________
- 30 min
- 60 min

**Time observed:**
- Observation ended: _______

**Observed challenge reaction**
- None
- Yes (list signs and symptoms)

**Time to onset:** ___________

**Observed challenge reaction treatment given**
- None
- Yes (list signs and symptoms)

**Delayed challenge reaction**
- None
- Yes (list signs and symptoms)

**Time to onset:** ___________

**Delayed challenge reaction treatment given**
- None
- Yes (list signs and symptoms)

---

Adapted from JAMA 2018; 321: 188-199
Sample Delabeling Letter

Name:

Date:

Summary from today’s visit:

This patient was assessed by a __________ at the ______ Hospital and

□ Is allergic to:
  a. This medication should be avoided
  b. We will update your hospital record with this allergy
  c. Your family doctor will be notified so that your medical record can be updated
  d. Please bring this letter to your pharmacist so that PharmaNet can be updated
  e. Other similar medications that should be avoided:

□ Is NOT allergic to:
  a. An oral drug challenge to drug:_________dose:______ was tolerated in the allergy clinic
  b. This medication may be prescribed again with no increased risk for adverse reaction above the baseline population.
  c. We will update your hospital and PharmaNet medical record
  d. Your family doctor will be notified so that your medical record can be updated
  e. You should monitor for any rashes over the next several days. Should a rash or other concerns arise, please contact our clinic. Delayed rashes are often bothersome but do not increase your risk of life threatening allergic reactions.

Follow up: ___________________

Sincerely,
## Sample Patient Pocket Card

<table>
<thead>
<tr>
<th>PENICILLIN Allergy Record</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NAME:</strong></td>
</tr>
<tr>
<td>[] Not Penicillin allergic</td>
</tr>
<tr>
<td>• Negative Penicillin Skin Test</td>
</tr>
<tr>
<td>• Negative penicillin rechallenge with:</td>
</tr>
<tr>
<td>Date: __________________</td>
</tr>
<tr>
<td>Signature: ________________ College</td>
</tr>
</tbody>
</table>

**ANTIMICROBIAL STEWARDSHIP PROGRAM**
Supplementary Materials
Penicillin – Minor Determinant Mixture – Compounding and Stability

Compounding and Stability Instructions for the following:
  a) Sodium hydroxide 0.114 N Solution (100 mL)
  b) Penicillin Skin Test #2 Reagent
  c) Penicillin Skin Test #3 Reagent
  d) Penicillin G – Minor Determinant – 1 mL vials (19 vials)

  a) Sodium hydroxide 0.114 N Solution (100 mL) - Predicted Expiry: 30 days
**BC PROVINCIAL ANTIMICROBIAL CLINICAL EXPERT (PACE) GROUP**

**BETA-LACTAM ANTIBIOTIC ALLERGY DELABELING GUIDELINE AND TOOLKIT**

<table>
<thead>
<tr>
<th>Item#</th>
<th>Item Description</th>
<th>Standard Qty</th>
<th>Qty to Use</th>
<th>Checked By</th>
<th>Item Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SODHP&lt;br&gt;Sodium Hydroxide Pellet 1 g</td>
<td>4.5600 g</td>
<td>4.5600 g</td>
<td>XENEX LABORATORIES INC</td>
<td>0.2300</td>
</tr>
<tr>
<td></td>
<td>Lot #:&lt;br&gt;Expire Date:</td>
<td></td>
<td></td>
<td>If Remainder:</td>
<td>Not assigned (Waste)</td>
</tr>
<tr>
<td>2</td>
<td>STER1&lt;br&gt;Water For Irrigation, Sterile &lt;None&gt;</td>
<td>150.0000 mL</td>
<td>150.0000 mL</td>
<td>BAXTER CORPORATION</td>
<td>0.1950</td>
</tr>
<tr>
<td></td>
<td>Lot #:&lt;br&gt;Expire Date:</td>
<td></td>
<td></td>
<td>If Remainder:</td>
<td>Not assigned (Waste)</td>
</tr>
</tbody>
</table>

**Unit Cost: $0.4250**<br>**Total: $0.4250**<br>**Total # of Items: 2**

**Directions:**

**PENICILLIN SKIN TEST REAGENT #1**
(SODIUM HYDROXIDE 0.114 N SOLUTION)

**MAKE UNDER LATEX FREE CONDITIONS**

**Formula:**

Sodium hydroxide NF 4.56g<br>Sterile water for irrigation 150mL

**Materials:**

100mL glass beaker X 2<br>100mL graduated cylinder X 2<br>glass stirring rod<br>PALL 25mm syringe filter with 0.2um Supor membrane HP1002 OR 0.22 mm filter unit (Milllex-GV OR Acrodisc-DLL)<br>100mL sterile empty vial<br>60mL syringe X 2<br>5mL syringe<br>PALL 25mm Hydrophobic Vent Filter HP2002

**Preparation Instructions:**

**MAKE UNDER LATEX FREE CONDITIONS**

**MAKE AS LATEX FREE**

**NOTE:** SODIUM HYDROXIDE IS VERY CORROSIVE. WEAR PROTECTIVE GOGGLES, MASK, GOWN, AND GLOVES AT ALL TIMES DURING PREPARATION.

**Have CHECKER check ALL WEIGHTS AND VOLUMES prior to mixing**

1. Clean all glassware (beakers, graduated cylinders, stirring rod) and triple rinse with sterile water for irrigation. Place in the laminar air flow hood.
2. Weigh out 4.56 grams of sodium hydroxide pellets using the scale in the dispensary compounding area. After the weight is checked, place in laminar air flow hood.

INSIDE LAMINAR AIR FLOW HOOD:
3. Add 40mL sterile water for irrigation to clean, rinsed 100mL beaker.

4. Add sodium hydroxide pellets to the water in the beaker.
NOTE: The solution will heat up as the sodium hydroxide dissolves.

5. When dissolved, carefully transfer the solution to the 100mL graduated cylinder. Rinse the beaker with small amounts of sterile water, and q.s. to 50mL with the rinse water. Drain beaker.

6. Transfer 50mL of concentrated sodium hydroxide solution back into beaker. Stir to mix.

7. Measure 95mL sterile water for irrigation in the second graduated cylinder. Transfer to second clean, rinsed beaker. To this add 5mL of the sodium hydroxide concentrate. Stir to mix.

8. Draw up the diluted sodium hydroxide solution into 2 X 60mL syringes (each syringe will contain 50mL).

9. Aseptically filter the dilute sodium hydroxide solution into an empty sterile 100mL vial through a Pall 0.2 micron filter (light blue). Vent the vial with a PALL 25mm hydrophobic vent filter unit HP2002.

10. Label vial and clean glassware and equipment used.
b) **Penicillin Skin Test #2 Reagent**

<table>
<thead>
<tr>
<th>Lot #</th>
<th>Expiry Date:</th>
<th>If Remainder:</th>
<th>Unit Cost:</th>
</tr>
</thead>
<tbody>
<tr>
<td>PENG11</td>
<td></td>
<td></td>
<td>$1.8455</td>
</tr>
<tr>
<td>02220261</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SODI.91</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>00037796</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Formula:**

Penicillin G Sodium 1 MU vial
Sodium Chloride 0.9% injection 10mL x 2

**Directions:**

- **MAKE UNDER LATEX FREE CONDITIONS**
- **MAKE UNDER LATEX FREE CONDITIONS**
- **MAKE AS LATEX FREE**

**Materials:**

- 10mL syringe x 2
- 1mL syringe
- 10mL sterile empty vial
- 25 gauge needles for venting vials

**Procedure:**

1. Add 8.2mL sodium chloride 0.9% injection (NS) to the 1 million unit vial of penicillin G sodium. Shake to dissolve. This will yield 119,000 units/mL (powder displaces 0.2mL).

2. Draw up 0.5mL of the 119,000 units/mL penicillin G sodium and add to 10mL sterile empty vial. To this add 9.5mL NS. Yields 10mL of a 0.01M solution.

3. Label with batch label.

**PREPARATION STABILITY:** 30 DAYS FROZEN
## Penicillin Skin Test #3 Reagent

<table>
<thead>
<tr>
<th>Item#</th>
<th>Item Description</th>
<th>Standard Qty</th>
<th>Qty to Use</th>
<th>Checked By Pkg. Size</th>
<th>Item Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NAOHSOLN Sodium Hydroxide &lt;None&gt; 0.114 N 00001926</td>
<td>8.2000 mL</td>
<td>8.2000 mL</td>
<td>SPH IV 100 ML BOTTLE</td>
<td>0.4048</td>
</tr>
<tr>
<td></td>
<td>Lot #:</td>
<td></td>
<td></td>
<td>Expiry Date:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>If Remainder: Waste</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>PENGI penicillin G Sodium Inj 1 MU 02220261</td>
<td>2.0000 mL</td>
<td>2.0000 mL</td>
<td>PHARMACEUTICAL PARTNERS OF CA 1 EA VIAL</td>
<td>1.2099</td>
</tr>
<tr>
<td></td>
<td>Lot #:</td>
<td></td>
<td></td>
<td>Expiry Date:</td>
<td>Not assigned [Waste]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>If Remainder:</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>SODI.9I Sodium Chloride 0.9% Inj 00037796</td>
<td>8.0000 mL</td>
<td>8.0000 mL</td>
<td>HOSPIRA HEALTHCARE CORP. 10 ML VIAL</td>
<td>0.3178</td>
</tr>
<tr>
<td></td>
<td>Lot #:</td>
<td></td>
<td></td>
<td>Expiry Date:</td>
<td>Waste</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>If Remainder: Waste</td>
<td></td>
</tr>
</tbody>
</table>

**Unit Cost:** $1.9325  
**Total:** $1.9325  
**Total # of Items:** 3

**Directions:**

PENICILLIN SKIN TEST REAGENT #3  
(BENZYL PENICILLOATE 0.02M + BENZYL PENICILLIN 0.02M SOLUTION)

**MAKE UNDER LATEX FREE CONDITIONS**  
**MAKE AS LATEX FREE**

* Have CHECKER check ALL WEIGHTS AND VOLUMES prior to mixing *

**Formula:**

Sodium Hydroxide 0.114N solution  
Penicillin G Sodium 1 MU vial  
Sodium Chloride 0.9% injection 10mL (should be placed in freezer day before manufacturing)

**Materials:**

- 10mL syringes X 2  
- 3mL syringe  
- 10mL sterile empty vial  
- ice bath (ice to be picked up the day before by D1 technician)  
- 25 gauge needles for venting vials

**Procedure:**

**MAKE UNDER LATEX FREE CONDITIONS**  
**MAKE AS LATEX FREE**

**NOTE:** Sodium chloride 0.9% injection (NS) 10mL vial can be placed in the IV Room freezer the night before manufacturing or in the morning before making. Check that D1 has picked up ice from CSICU the day before as the final product needs to be kept ice cold.
1. Add 8.2mL sodium hydroxide 0.114N solution to the penicillin G sodium 1mU vial. Shake to dissolve. Wait for 5 minutes, then proceed IMMEDIATELY with the next step.

2. Draw up 8mL ice cold sodium chloride 0.9% injection (see note above about placing NS vial in freezer beforehand) and add to the 10mL sterile empty vial. Draw up 2mL of the penicillin G sodium/sodium hydroxide solution and transfer into the sterile vial containing 8mL of ICE COLD normal saline. This will provide a 0.02M solution of each of benzylpenicilloate and benzylpenicillin. NOTE: Benzylpenicilloate breaks down quickly at room temperature. Immediately after preparing this reagent, the Penicillin Minor Determinant Skin Test solution must be prepared.

3. Label with batch label and ask checker to check immediately. Place in a small zip-lock bag back in the ice bath until ready to prepare the Penicillin Minor Determinant Skin test solution.

PREPARATION STABILITY: 30 DAYS FROZEN
d) **Penicillin Minor Determinant Skin Test –**

<table>
<thead>
<tr>
<th>Item#</th>
<th>Item Description</th>
<th>Standard Qty</th>
<th>Qty to Use</th>
<th>Checked By</th>
<th>Item Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Manufacturer</td>
<td>mL</td>
<td>Pkg. Size</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>PENGTEST#2 Penicillin Skin Test #2 Reagent</td>
<td>9.5000</td>
<td>9.5000 mL</td>
<td>SPH IV</td>
<td>1.8455</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lot #:</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>PENGTEST#3 Penicillin Skin Test #3 Reagent</td>
<td>9.5000</td>
<td>9.5000 mL</td>
<td>SPH IV</td>
<td>1.9325</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lot #:</td>
<td></td>
</tr>
</tbody>
</table>

**Unit Cost:** $0.1988  **Total:** $3.7780  **Total # of Items:** 2

**Directions:** **PENICILLIN MINOR DETERMINANT SKIN TEST**  (BENZYPENCILLOATE 0.01M + BENZYLPERCILLIN 0.015M)

**BEFORE MANUFACTURING THE SKIN TEST, YOU MUST FIRST MANUFACTURE THE FOLLOWING:**

**** Make under LATEX FREE conditions **  ** Make as LATEX FREE **

1. Sodium Hydroxide 0.114N Solution (Penicillin Skin Test Reagent #1) Saved as: NAOHSOLN
2. Penicillin Skin Test Reagent #2. Saved as: PENGTEST#2
3. Penicillin Skin Test Reagent #3. Saved as: PENGTEST#3

**Formula:**
Penicillin Skin Test Reagent #2 10mL
Penicillin Skin Test Reagent #3 10mL

**Materials:**
2mL sterile empty vials X 19 (OMEGA brand and Allergy Laboratories, Inc. brands are latex free)
3mL syringes X 4
25 gauge needles
20 gauge needles

**Procedure:**

**MAKE UNDER LATEX FREE CONDITIONS **  ** MAKE AS LATEX FREE **

* NOTE: Ensure ice is available (on the day before manufacturing Penicillin Skin Test Reagent #3 10mL, the technician checker or d technician should ask D1 technician to pick up ice from CSICU during their afternoon delivery. Ice should be stored overnight in the IV Room freezer *

1. Immediately after preparing Penicillin Skin Test Reagents #2 and #3, draw up reagent #2 into a syringe (2.5mL = 5doses at a time), and add 0.5mL to each 2mL vial. Use 25 gauge needles to vent the vials.
2. Remove reagent #3 from the ice bath and draw up 2.5mL (5 doses) into a syringe, adding 0.5mL to each of the vials containing 0.5mL of reagent #2.

3. Label immediately and place in freezer.

PREPARATION STABILITY: 30 DAYS FROZEN

Auxiliary label: LATEX FREE (ensure it has been made under latex free conditions)

10 VIALS TO BE SENT TO VGH:
Advise the IV Room Packager and they will send the vials to VGH the next day with the usual IV Run. IV Room Packager: The vials should be packaged up in a styrofoam cooler with lots of ice packs and bubble wrap. Label the cooler with the VGH address and "STORE IN FREEZER UPON ARRIVAL" warning.
# BC Provincial Antimicrobial Clinical Expert (PACE) Group

## Beta-lactam Antibiotic Allergy Delabeling Guideline and Toolkit

### Request to Inactivate Adverse Reaction/Clinical Condition on PharmaNet Profile

The request to inactivate text in the Adverse Reaction/Clinical Condition was initiated by:
- [ ] Patient
- [ ] Patient’s Representative (specify name and relationship to patient)
- [ ] Doctor
- [ ] Pharmacist
- [ ] Other (specify)

The identity of the request initiator was verified by:
- [ ] BC Services Card
- [ ] Driver’s License
- [ ] Other (specify)

### Patient Information

<table>
<thead>
<tr>
<th>Patient Last Name</th>
<th>Patient First Name</th>
<th>Personal Health Number</th>
</tr>
</thead>
</table>

### Pharmacy Information

<table>
<thead>
<tr>
<th>Pharmacy Name</th>
<th>PharmaCare Code</th>
<th>Phone Number</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Pharmacist Name</th>
<th>Registration Number</th>
</tr>
</thead>
</table>

### PharmaNet Profile Change

Text to be inactivated

Justification for Inactivation

### Pharmacist Signature

<table>
<thead>
<tr>
<th>Pharmacist Signature</th>
<th>Date Signed</th>
</tr>
</thead>
</table>

Fax this form to the PharmaNet Data Quality Services Team at 250 953-0486

This form contains confidential information intended only for PharmaNet Data Quality Services. Any other distribution, copying or disclosure is strictly prohibited. If you have received this fax in error, please write "MISDIRECTED" across the front of the form and fax to 1 250 953-0486, then destroy the pages received in error.

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HETH 5559 2017/03/17